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Excitability and Functional Organization within a Peripheral Tactile Unit

BY

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INTRODUCTION

A peripheral sensory unit—that is, a cell in the dorsal root ganglion and its processes—generally innervates a certain area of the skin known as the receptive field of the unit. The area of sensitivity is extended through peripheral branching of the afferent fibre. Within each receptive field there will therefore be several receptive nerve-endings converging to the same afferent fibre. In their studies of touch receptors in the frog's skin CATTELL and HOAGLAND (1931) found that the impulse discharge elicited by mechanical stimulation of one half of the receptive field was reduced by preceding stimulation of the other half. They ascribed this inhibitory interaction to antidromic discharge in the peripheral branches of the afferent fibre. In the cat TOWER (1940) observed a similar interaction for corneal units activated by mechanical stimulation. She found that adequate pressure applied anywhere in the receptive field of a spontaneously active fibre was followed by a depression of the spontaneous activity. Tower also found evidence of a differentiation of the excitability within the unit, the threshold being lower and the adaptation slower in the centre of the receptive field than at its periphery.

The present paper describes a quantitative analysis of the excitability within the receptive field of a cutaneous sensory unit and the integration of activity elicited in various peripheral branches of a single afferent fibre. Touch units in the toad were chosen for the analysis. The receptive fields of most of these units consist of a number of small well-defined areas on the skin, the deformation of which elicits a discharge in the afferent fibre. The sensitive areas are usually more or less point-like and the fact that they are separated by insensitive skin affords an opportunity to stimulate subdivisions of one unit individually.

A method of mechanical stimulation was worked out which made it possible to measure the excitability at single sensitive points. To ascertain whether there is a spatial discrimination mechanism within a single unit, measurements were made of the threshold and

latency of the response on stimulation at the various points innervated by a particular afferent fibre.

The changes in threshold produced at a sensitive point by conditioning stimulation of this or other points in the same field were measured. This procedure was essential for the study of the integration of activity elicited in various peripheral branches of a single afferent fibre.

Two sensitive points belonging to the same unit were subjected simultaneously to repeated stimulation, each point by a separate stimulator, and the impulse frequency of the resulting discharge in the afferent fibre was determined. In another series of experiments, in which the stimulation was performed by manual touch, the duration and impulse frequency of the afferent discharge was determined and the values for individual and simultaneous touch of two points innervated by the same unit were compared.

The possibility of an interaction between different units was examined by measuring the excitability in units with overlapping receptive fields.

Some of the principal results have been published in a preliminary report (LINDBLOM 1957).

PREVIOUS INVESTIGATIONS

SURVEYED WITH SPECIAL REFERENCE TO PROPERTIES OF TOUCH RECEPTORS IN THE FROG AND THE TOAD

Discharge characteristics. The first to study discharges from touch receptors by recording directly from the afferent fibres were ADRIAN and ZOTTERMAN (1926a) in their classical study of the properties of sensory nerve-endings. Recording from thin branches of the digital nerves of the cat they found that tactile stimuli elicited high-frequency discharges, which adapted rapidly. More detailed information on the characteristics of touch receptors was obtained by ADRIAN, CATTELL and HOAGLAND (1931). These authors studied the response in single units in the frog by recording the antidromic discharge in a branch of the afferent fibre. The cutaneous area innervated by the other branches of the same fibre was stimulated mechanically by means of air blasts of controlled duration and frequency. A slight, transient displacement of the skin was sufficient to elicit a discharge; on repeated stimulation a frequency of 200 impulses per second or even more could be reached for short periods, and a fairly high frequency could be maintained for several seconds. On application of a continuous air blast the discharge adapted rapidly and the response was reduced to one or two impulses if the stimulus was applied suddenly; it was tentatively concluded that impulses are set up only during the actual movement of the skin. The same type of unit has been recognized in the toad by MARUHASHI, MIZUGUCHI and TASAKI (1952) ("phasic tactile fibres"). These authors also observed the pointed distribution of the sensitivity in the receptive fields of the tactile units in this animal.

Variations in receptor excitability. It is well known that the adaptation and the excitability of sensory endings, among them touch receptors in the frog, may be influenced by changes in the chemical environment (FENG 1933; TALAAT 1933; HOAGLAND 1936; ECHLIN and PROPPER 1937; *cf.* MATTHEWS 1931 and FITZGERALD 1940). HABGOOD (1950) has found that the sensory

receptors in the frog's skin are sensitized by electrical stimulation of the afferent nerve. He ascribed this effect to a substance released at the endings by antidromic impulses. Sympathetic stimulation causes a lowering of the threshold and a slowing of the adaptation in the frog's touch receptors by way of efferent sympathetic fibres contained in the skin nerves, as has been revealed by LOEWENSTEIN (1956a). The same author has also demonstrated that these receptors are readily excited and adapt more slowly when the skin is stretched (LOEWENSTEIN 1956b).

Afferent fibres. MATTHEWS (1929) found that impulses released by mechanical stimulation of the frog's skin—including light contact—were conducted at a velocity of about 15 metres per second, and the fibres concerned were classified as A-beta fibres according to ERLANGER and GASSER (1924). By means of an indirect method HARRIS (1935) obtained evidence that tactile discharges in the frog are conducted at various velocities between 5 and 45 metres per second, that is, in the whole range of A fibres. MARUHASHI et al. (1952) measured the diameter of the tactile fibres included in a sample of dissected single-fibre preparations in the toad and found that it ranged from about 8 to 15 μ. These fibres were the largest afferents from the skin and the conduction velocity was 20—35 metres per second.

Microanatomy. ADRIAN et al. (1931) deduced that the touch receptors are situated in the epidermis since the tactile discharges could not be elicited after it had been removed. This was confirmed by RUBIN and SYROCKI (1936) who identified the touch receptors as free nerve-endings in the epidermis. Their study was performed on frogs but it is highly probable that the touch receptors in the toad also consist of free endings. There are numerous such endings in the epidermis of both the frog and the toad, and no essential difference in the innervation of the skin of these two animals seems to have been recognized (see MERKEL 1880 and WHITEAR 1955).

The epidermal endings may display bulb-like or varicose swellings at the extreme distal portion (RETZIUS 1892; EBERTH and BUNGE 1893; HULANICKA 1912; WHITEAR 1955). More or less specialized end-organs have been described that might be involved in the reception of tactile stimuli—such as Merkel's "tactile

maculae" and Eberth and Bunge's "Endzellen" (see GAUPP 1904). However, since none of these end-organs appears to have been consistently found, it is difficult to assess their significance. RUBIN and SYROCKI (1936), in their reinvestigation of sensory endings in the frog's skin, found only free and bulb-like endings, and in the recent study by WHITEAR (1955) on the skin of the frog and the toad only free and varicose endings are described.

The picture of the peripheral ramification of cutaneous medullated fibres in the frog and the toad is one of dichotomizing fibres which diminish in thickness and finally lose their myelin sheaths (RETZIUS 1892; CAJAL 1909; BOEKE 1932; WHITEAR 1955). A subepidermal plexus has been described in the frog (see EBERTH and BUNGE 1893), although it does not seem to have been determined whether the plexus in this animal is a true one with anastomoses or if it is made up of interlocking branches (*cf.* WEDDELL 1941).

Other types of mechanoreceptors. The present investigation was confined to the common low-threshold, rapidly adapting type of touch receptor. Other types of mechanoreceptors, which have been recognized in the skin of the frog and toad, may, however, be briefly mentioned. FESSARD and SEGERS (1942) have differentiated a second type of touch receptor in the frog's skin that is less rapidly adapting. Slowly adapting receptors responding to pressure or stretch have been demonstrated in both animals (BRONK 1929; HOGG 1935; RUBIN and SYROCKI 1936; MARUHASHI et al. 1952; LOEWENSTEIN 1956b; CATTON 1958). Usually these receptors, which are subepidermal, have a higher threshold and are connected to finer fibres than the tactile endings, although some of them appear to have a low threshold and to discharge on touch also ("tonic tactile fibres" of MARUHASHI et al. 1952).

METHODS

Preparation of the animals. All the experiments were performed on toads collected in Sweden (*Bufo bufo*) and weighing from 30 to 70 g. The animals were decerebrated under ether and held in position in a trough by means of pins clamped against the vertebrae and the pelvic ring. Disturbing spontaneous or reflex movements were controlled with curare (Tubocurarin, Vitrum; repeated doses of 0.1—0.2 ml, administered subcutaneously). The viability of the preparations was checked by testing the reflex excitability and by microscopic inspection of the circulation in the vessels on the surface of the spinal cord.

After laminectomy a dorsal root, generally the ninth, which innervates the plantar surface and the back of the hindleg, was freed as near the spinal cord as possible. The root was lifted on to a bakelite plate and split into thin filaments from the severed end. The dissected filaments were covered by Ringer's solution, which was continuously renewed.

The experiments were carried out at room temperature. The temperature of the skin on the hindlegs of the toads, measured by means of small thermocouples, was between 18 and 21°C, and in the trunk muscles it ranged from 20 to 23°C.

The receptive fields were copied from photographic plates exposed through the dissecting microscope after marking the sensitive points with lacquer.

Recording. Monopolar recordings of the action potentials were made from the end of the dorsal root filament. To obtain single unit responses of a significant amplitude various methods of increasing the external resistance were tried. The air-gap technique (see TASAKI and MIZUGUCHI 1948) proved the most suitable. It was applied in the following manner. The end of the filament was lifted on to a recording electrode, which was adjusted so that there was a small air gap between the electrode and the Ringer film on the dissection plate. The bowl-shaped Ag-AgCl electrode was filled with Ringer's solution and covered to reduce evaporation. In

control experiments the resistance of the part of the filament passing through the air gap was from 4 to 10 megohms. The trough and the toad were earthed and the second electrode was dipped in the Ringer's solution close to the dissected filaments. A 20 megohm variable resistance connected in series with this electrode could be adjusted for each filament so as to prevent amplification of disturbing signals of the same phase that were picked up by the electrodes. The latter were connected through condensers to a differential amplifier (HAAPANEN 1953), the input resistance of which was 4 megohms (time constant 10 msec). The amplifier was connected to a cathode-ray oscilloscope. The responses were photographed from a second tube by single exposures or on continuously moving film. The all-or-none character and the constant shape and amplitude of the response provided evidence that this was picked up from single units. The discharges were also transformed into an audible signal.

With this recording technique most of the fibres remained active for from one-half to 4 hours. Towards the end of this period the spike potentials generally decreased in amplitude owing to deterioration at the recording site. Some fibres ceased to give a response only a few minutes after the filament had been raised on to the electrode; this would be expected if a node of the active fibre happened to lie in the air gap.

Mechanical stimulation. The skin was stimulated mechanically (i) by stroking with a brush or by touching with a small blunt rod, and (ii) by means of a specially designed stimulator. Two such instruments were used in order to enable two points on the skin to be stimulated independently.

The design of the stimulator is shown in Fig. 1. A narrow blunt metal rod *(in black)*, 0.3 mm in diameter, was mounted on the cone of a moving-coil loudspeaker (flux density 11,000 gauss) so as to follow the movements of the diaphragm. The rod was affixed to the extreme end of a lever of perspex, which projected beyond the rim of the loudspeaker. This enabled the rods of the two stimulators to be brought close together so that adjacent points on the skin could be stimulated. Each of the two instruments was placed on a micro-manipulator to facilitate accurate adjustment of the rods. Mechanical pulses, single or repeated, were produced by

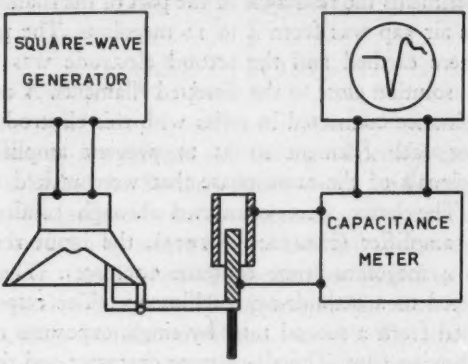

Fig. 1. Mechanical stimulator and apparatus for recording wave form of stimulus.

means of square-wave pulses with a duration of 1.0 or 1.5 msec, which were fed to the loudspeaker. Two square-wave pulse generators were used, these being connected to the same, or each to one, mechanical stimulator. A third square-wave pulse generator was used for electrical stimulation of the dorsal root.

Wave form of mechanical stimulus. The arrangement for recording the amplitude and form of the pulses produced by the mechanical stimulator is also shown in Fig. 1. On the upper edge of the rod of the stimulator a small metal tube was fixed which was freely fitted into another, wider tube fixed to the rim of the loudspeaker. For the variable co-axial condenser so formed the variation in capacitance is theoretically proportional to the axial displacement of the inner tube. By connecting this to a capacitance meter (DICKINSON 1950, p. 113) of sufficiently high sensitivity and rapid response (rise time approximately 0.2 msec), the axial motion of the rod could be studied on the oscilloscope. The recorded variation in capacitance gave a true representation of the motion of the rod as observed under the microscope in stroboscopic light. A calibration curve was drawn by means of which the photographed capacitance changes could subsequently be converted into amplitude of movement. The amplitude was estimated to the nearest 5 μ on the microscope scale. By varying the strength of the

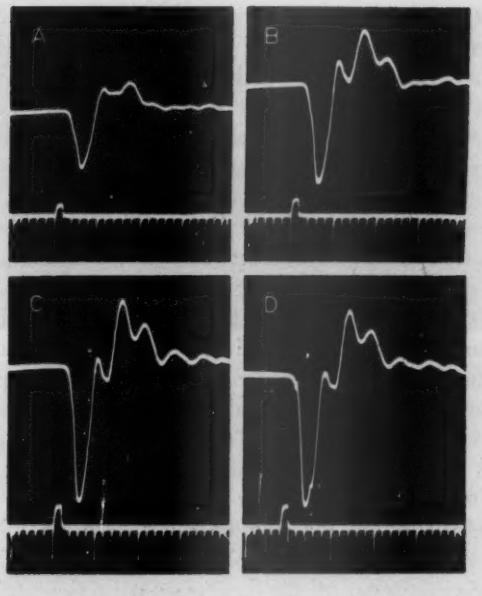

Fig. 2. Capacitance curves illustrating wave form of mechanical stimulus. *A, B, C:* Various stimulus strengths; stimulator rod moving in air. *D:* Same stimulus strength as in *C;* stimulator rod applied just above the skin. Displacement of skin surface begins at kink indicated by upper arrow; contact between rod and skin is broken at lower arrow. Time: 1 and 5 msec. Vertical scale line: 100 μ.

electrical pulse, any amplitude of movement between 0 and 500 μ could be obtained.

The capacitance records in Fig. 2 illustrate the motion of the stimulator rod for single square-wave pulses of 1.0 msec. A downward deflection indicates a downward movement of the rod towards the skin. Owing to the delay and distortion in the stimulator circuit, which also contained transformers, the movement of the rod began about one millisecond later than the electrical pulse marked on the time scale. For the same reasons, and owing to the inertia of the mechanical system, the slope of the mechanical pulse was less steep than that of the electrical pulse. However, the peak was reached within 2 msec. A comparison of Figs. 2*A, B* and *C* for downward deflections of 80, 125, and 180 μ, respectively,

shows that the rise time was approximately the same for the various amplitudes. The rod described residual oscillations of various superimposed frequencies, which disappeared in 10—20 msec, depending on the strength of the stimulus.

Displacement of skin. In order to avoid interference from the residual oscillations the mechanical stimulator was adjusted so that the tip of the rod was just above the surface of the skin. To ensure accurate determination of the amplitude of the skin displacement a small battery-charged condenser (22 $\mu\mu$ F) was connected to the rod. When the rod made contact with the skin the condenser discharged, a record of this event being superimposed on the capacitance curve. This is illustrated in Fig. 2*D*, in which the small kink in the downward deflection *(upper arrow)* was produced on the discharge of the condenser and therefore marks the beginning of the displacement of the skin. The vertical distance between the kink and the maximum deflection thus represents the amplitude of the displacement. When the rod returns after its maximum downward deflection the skin does not keep up with it. The moment when the rod and the skin lose contact is indicated by a kink in the return half of the downward deflection as the condenser charges *(lower arrow)*.

The form of stimulation used was thus a displacement of the skin produced by a mechanical pulse of short duration. The amplitude of the displacement was used as a measure of the intensity of the stimulus and was determined for each stimulation from the recorded and photographed capacitance deflections.

The mechanical pulses were found to activate the tactile units when they were applied at any angle from the vertical almost to the tangent to the skin. However, in order to ensure that the results would be comparable only the vertical direction was used in the actual experiments. Stretching of the skin was avoided in experiments with threshold determinations in case this should prejudice comparison (see LOEWENSTEIN 1956b).

Fig. 3 illustrates the displacement caused by the stimulator. The skin is represented by photographic silhouettes of three adjacent warts at a magnification of 20. *A* and *B* were exposed in stroboscopic light with flashes of 0.06 msec duration triggered synchronously at the maximum displacement. Each plate was exposed

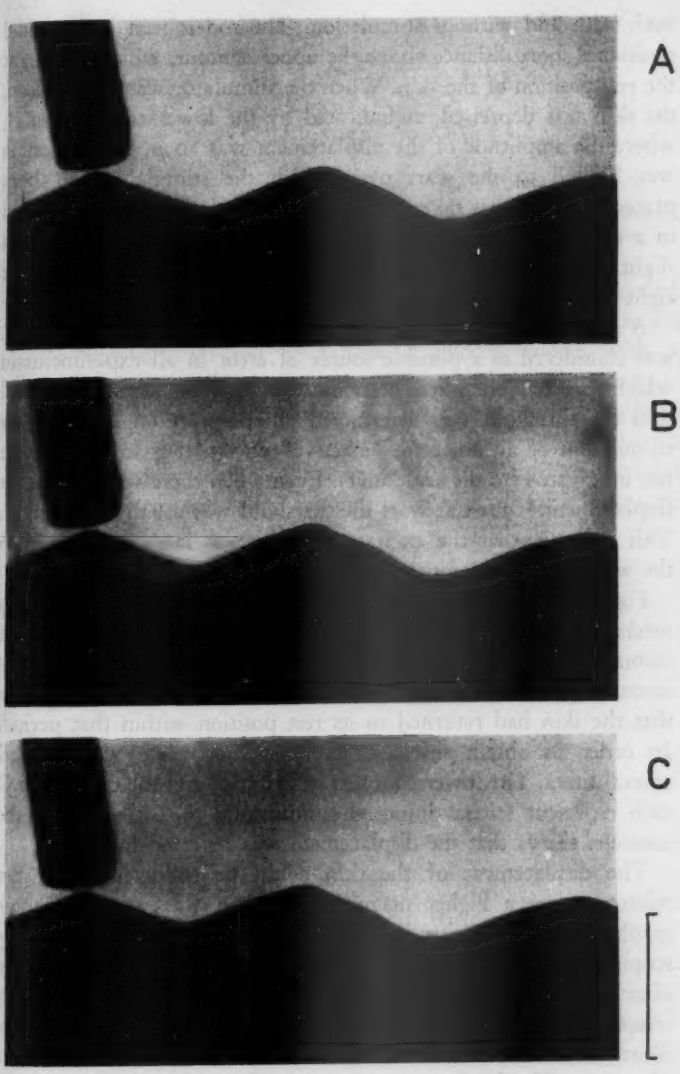

Fig. 3. Photographic silhouettes of three skin warts and stimulator rod. *A* and *B* illustrate displacement of skin surface (indicated by double contours) at two different stimulus strengths. *C:* No visible displacement 3 msec after maximum downward deflection; same stimulus strength as in *B*. Scale line: 1 mm.

both with and without stimulation. The rod is seen in its initial position a short distance above the upper contour, which represents the rest position of the skin. When the stimulator was switched on, the skin was depressed, as indicated by the lower contour. In *A*, where the amplitude of the displacement was 80 μ, the depression was limited to the wart over which the stimulator had been placed. Fig. 3*B* was taken on stronger stimulation, which resulted in a displacement of about 200 μ beneath the rod, but also in a slight depression of the adjacent wart; the wart on the extreme right was still unaffected.

A spatial distribution of the displacement, illustrated in Fig. 3*B*, was considered as a possible source of error in all experiments in which the excitability was determined in adjacent warts. In control tests the threshold was determined at one wart on simultaneous stimulation of an adjacent, "inactive" one (that is to say, a wart not innervated by the same unit). Even when there was a transient displacement at the test wart the threshold was usually unchanged. This indicates that the excitatory effect was largely confined to the wart that was compressed by the stimulator rod.

Fig. 3*C* was likewise exposed in stroboscopic light, both with mechanical stimulation at the same amplitude as in *B*, and without stimulation; in this case the exposure was made 3 msec after maximum displacement. The absence of double contours in *C* indicates that the skin had returned to its rest position within that period. In order to obtain sufficient contrast each plate was exposed several times. The lower contours in *A* and *B* and the contour in *C* each represent several hundred stimuli, and the sharpness of the contours shows that the displacement was repeated identically.

The displacement of the skin could be followed under the microscope at a higher magnification than was possible photographically, and was studied in this way with the aid of stroboscopic illumination of the skin silhouette at various short intervals after the maximum deformation. The curves in Fig. 4 have been selected as representative of a series of such determinations; they illustrate the recovery of the skin after a maximum displacement of 250 μ. The horizontal axis *RP* indicates the rest position. It is seen from the curves that only about one-fifth of the deformation (50—65 μ) remained after one millisecond. Although recovery

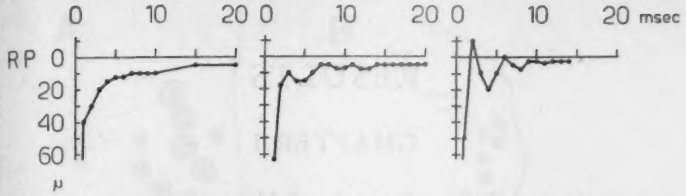

Fig. 4. Various types of recovery of skin surface after single displacement of 250 μ. Maximum displacement at zero time. *RP:* rest position of skin.

from deformation was nearly complete after 3 msec, a slight deviation was still visible after 20 msec. In the left curve in Fig. 4 the recovery is seen to follow a smooth course with an asymptotic approach to the rest position. Not infrequently, a damped oscillation was superimposed on this curve, its amplitude varying from very low, as illustrated by the middle curve, to fairly marked, as in the right curve. The frequency of the oscillation, however, was fairly constant from case to case at 200—250 cycles per second.

RESULTS

CHAPTER I

Receptive fields

The material consisted of 190 tactile units altogether. Units with their receptive fields on the plantar surface of the foot and the back of the lower leg were chosen primarily because these regions were most easily accessible to stimulation by means of the mechanical stimulator. A few units on the dorsum of the foot and on the upper leg were also examined.

The receptive fields were located by lightly stroking the skin on the hindleg, and then mapped by point stimulation. The fields of most units consisted of a number of small, point-like, sensitive areas, separated by insensitive skin. Between 2 and 29 such points were innervated by a single unit. They were distributed within an area ranging from 2 to 35 sq. mm; there was a slight predominance of fields below 15 sq. mm and most of them had from 2 to 12 sensitive points. These were generally located on the wart-like elevations of the skin, one on each wart.

The various warts innervated by a particular fibre lay near one another although "inactive" warts were sometimes interposed, especially at the periphery of the field. The configuration of the receptive field was generally irregular, as is illustrated in Figs. 5*A* and *B*, which show the sensitive warts of two units located on the back of the lower leg *(A)* and on the plantar surface near the lower joint *(B)*. The warts belonging to the unit in Fig. 5*C*, lying on the distal part of the plantar surface, were contained in an oval area. However, a smooth field contour such as this was too rare to be regarded as characteristic.

Apart from the irregular contour, the only recurrent feature of the field configuration was an elongation in the direction of the leg. The length of the fields was on average twice the width but the extent of the elongation varied considerably. The sketch in Fig. 5*D* shows a field on the distal part of the plantar surface

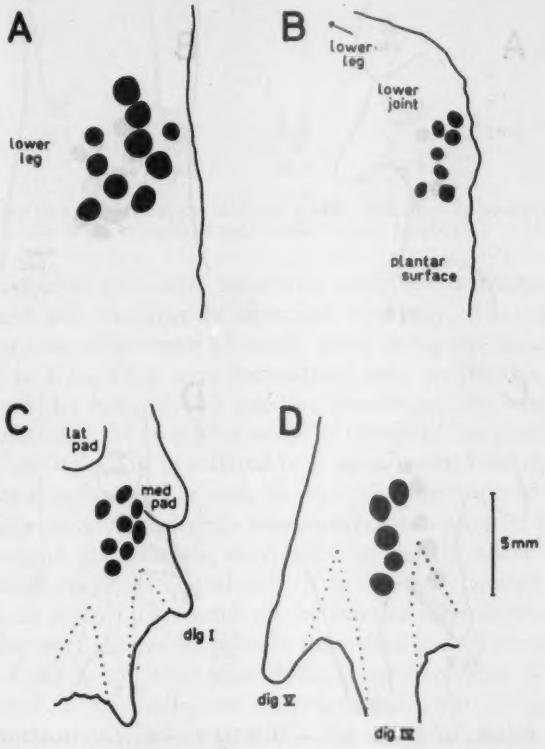

Fig. 5. Sketches of lower leg and plantar surface showing receptive fields of four tactile units. Filled contours in each sketch are warts, all of them innervated by one dorsal root fibre.

consisting of 5 warts in a fairly straight line. Long narrow fields such as this were found chiefly along the lateral and medial borders of the foot and along the digits (see also Fig. 6*C*).

In regions where the warts were sparse, as, for instance, on the digits and web, the receptive fields included both warts and well-defined sensitive areas located on adjacent smooth parts of the skin. Four such units, all of them located on the plantar surface, are shown in Figs. *6A-D*, where the sensitive areas that do not lie on warts are hatched. Most of these areas were quite small and usually more or less point-like, as were those situated on warts.

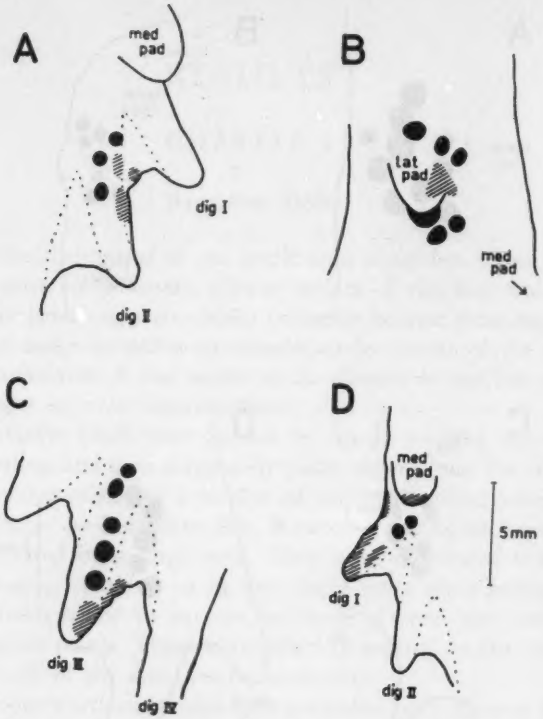

Fig. 6. Sketches of plantar surface showing four receptive fields comprising sensitive areas (hatched) on plain skin.

In view of the histologic data on the peripheral ramification of sensory neurons in the skin (p. 9) and the punctate distribution of the sensitivity within the receptive fields, it is reasonable to assume that each sensitive point is innervated by one branch of the afferent fibre. One sensitive wart or small sensitive area on plain skin is evidently the smallest part of a receptive field that can be separately activated by natural stimulation, and from a *functional aspect* it may therefore be regarded as a single receptor. In the present study, the term receptor has thus been used to denote the part of a unit—presumably the naked ending of a branch of the afferent fibre—that is responsible for the property of mechano-reception displayed by a sensitive point.

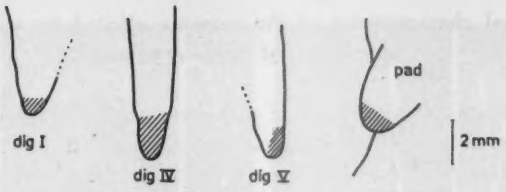

Fig. 7. Sketches of three digits and one medial pad showing receptive fields of four tactile units of apical type. Sensitive areas hatched.

A number of units were found that constituted a distinct group and these will therefore be described separately. The receptive fields of these units were all small, being about one square millimetre in area. They were encountered only on the tips of the digits and the poles of two pad-like formations, one lateral and one medial, that lie on a level with the middle of the plantar surface. These units will be referred to as *apical units*. Four examples are shown in Fig. 7. The unit on *dig. I* has the form of a cap. The fields were often slightly asymmetrical in relation to the tips of the digits; for example, they might be slightly wider on the plantar side, as in the case of *dig. IV* in Fig. 7, or located to one side, as on *dig. V*. The sketch on the extreme right shows a field extending over the caudal pole on the medial pad. The receptive fields of the apical units were diffusely sensitive and, as far as their small size permits one to judge, there was no punctate distribution of the sensitivity within the individual fields.

CHAPTER II

1. General characteristics of the response elicited by mechanical stimulation of single receptors

For each mechanical pulse of sufficient amplitude applied to the skin over a particular receptor, a single action potential was recorded in the dorsal root fibre. Even when the stimulus strength was above threshold a single impulse was obtained; only in a few cases did strong supraliminal stimulation give rise to two impulses per stimulus in the same fibre. Fig. 8 shows responses elicited in a tactile fibre, the receptive field of which was located on the medial pad. The amplitude of the stimulus used is shown by the capacitance curve to the right of each record from the dorsal root filament. *A* shows the response to a single stimulus of threshold strength; it is seen that the impulse appears about 10 msec after the shock artefact, which marks the beginning of the square-wave pulse fed to the mechanical stimulator. *B-E* illustrate stimulation at different intensities, and the lefthand record in each figure represents the superimposed dorsal root fibre responses from 6 consecutive stimuli of constant amplitude, delivered at a frequency of one per second. In *B*, where the amplitude of each stimulus was 40 μ, stimulation was subliminal and no response was obtained. An increase in the intensity to 50 μ, as in *C*, was sufficient to elicit an impulse at each stimulation. The lowest amplitude to elicit a response to each of at least 6 consecutive stimuli delivered at a low frequency—usually one per second—will be referred to as the *threshold* for the point or receptor.

It is well known from studies on various types of receptors that the latency of the response may be reduced with increasing intensity of the stimulus. This applied also to the receptors under study and was studied in some detail as a basis for subsequent latency measurements. As in Fig. 8*C*, the latency of the response varied slightly on stimulation at threshold. If the stimulation was slightly supraliminal, as in *D*, where the amplitude was 55 μ, the response occurred at a constant latency. A further rise in stimulus strength resulted in a gradual decrease of the latency to a minimum. The shortest latency for the receptor illustrated in Fig. 8 was 7 msec (*E*), the required amplitude in this case being 120 μ. The gradual shift of the latency on varying the stimulus strength is

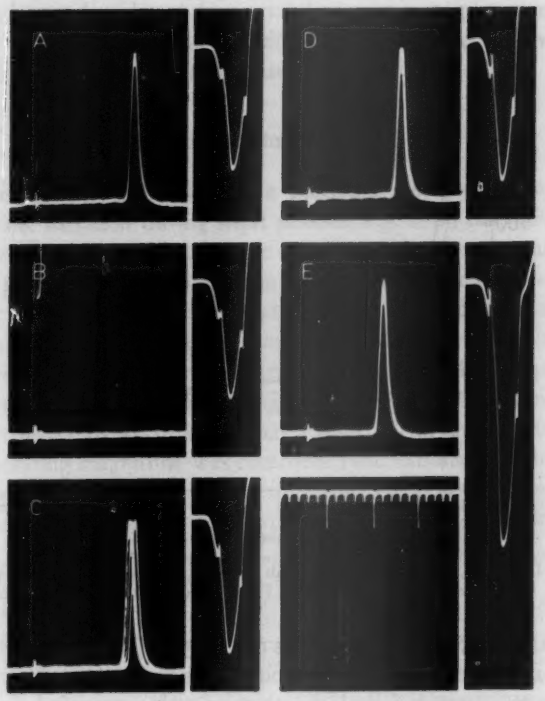

Fig. 8. Dorsal root fibre responses following stimulation of tactile receptor with short mechanical pulses; stimuli are shown to the right of each dorsal root record. *A:* Response to single stimulus of threshold strength. *B—E:* Effect of increasing stimulus strength; each figure shows the superimposed dorsal root fibre responses from six consecutive stimulations. Time: 1 and 5 msec. Lefthand vertical scale line: 0.5 mV. Righthand vertical scale line: 50 μ.

illustrated by the curve in Fig. 9, which is from another receptor. The shortest latency at strong supraliminal stimulation was 10.3 msec *(vertical broken line)*, and reduction of the stimulus strength resulted in an increase in latency along a curve of the hyperbolic type. The maximum latency of 15.8 msec occurred at threshold, 110 μ *(horizontal broken line)*. The curve in Fig. 9 is similar to that obtained by GRAY and MALCOLM (1951) for touch receptors in the frog, and also to that for pacinian corpuscles in the cat's mesentery (GRAY and MALCOLM 1950; ALVAREZ-BUYLLA and DE

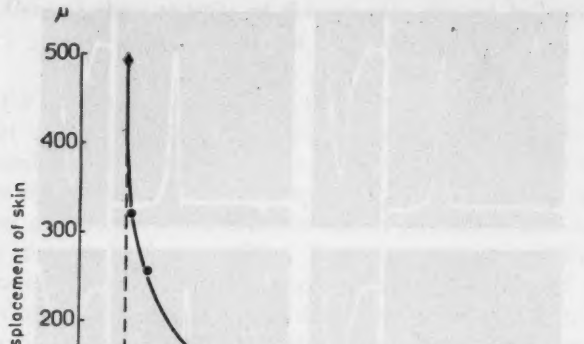

Fig. 9. Diagram showing variation in latency of response with stimulus strength (amplitude of displacement). From apical unit on medial pad.

Arellano 1953; Gray and Sato 1953). The shortest latency values obtained at the various points innervated by a particular fibre were compared and the shortest value recorded for each unit in a series was used for calculating the conduction velocity (p. 29).

A latency variation of 5—6 msec, that is, of about the same magnitude as that illustrated in Fig. 9, was observed for several receptors, but for many of them the variation was smaller, down to one millisecond; the mean of a large number (70) was 2.5 msec. The increase in the gradient of the mechanical pulse at high stimulus strengths (Fig. 2) should be accompanied by a shortening of the latency on supraliminal stimulation (*cf.* Catton 1958), though apparently only by a fraction of one millisecond, since the change in the rate of rise was slight. Practically the whole latency variation therefore represents a delay in the initiation of the propagated impulse. Since most of the recovery of the skin takes place within 1—2 msec (Fig. 4) the observed delays, especially the longer ones,

are evidence of a change in excitability at the receptor that has a longer time constant than the displacement of the skin surface. (For further discussion of the latency, see p. 66.)

2. Variations in threshold with time

Generally the threshold for a particular receptor showed no significant variation during short periods, *e.g.* from one minute to another. The thresholds of some receptors were constant also for longer periods of one-half to one hour, while other receptors displayed varying values. The variations often appeared as a smooth moderate rise—for example, from 60 to 70 μ over half an hour. Marked fluctuations were sometimes observed that implied a doubling of the threshold during the same period—for instance, a rise from 35 to 75 μ. Less often a lowering of the threshold of corresponding magnitude was recorded. Fluctuations in both directions were sometimes seen for the same receptor—for instance, from 90 to 100 and back to 85 μ during the course of half an hour.

Accuracy of threshold determinations. Before describing the attempts made to analyse the mechanism underlying the threshold fluctuations, an account will be given of how threshold differences were evaluated. The accuracy in determining the amplitude of the displacement of the skin was estimated to be within 5 μ. Threshold differences greater than 5 μ were, however, not necessarily significant from a physiological aspect. The thresholds were determined by increasing the strength of the stimulus in small increments until an impulse was elicited. Owing to the all-or-none character of the response it could not be seen whether the intensity of the stimulus was slightly supraliminal or at threshold unless detailed measurements of the latency were performed (*cf.* p. 22), or unless fine supra- and subliminal adjustments were made with the intensity control of the square-wave generator. In experiments where a large number of threshold determinations were performed is was found expedient to limit the time spent on each determination in spite of the fact that this enhanced the risk of erroneous setting. In consequence, although they might exceed 5 μ, differences in readings that were relatively small were not regarded as significant from a physiological aspect unless they recurred in several tests.

The threshold fluctuations with time cannot be attributed to inaccurate setting of the stimulus intensity. Repeated determinations showed a gradual shift of threshold, and fluctuations occurred also in experiments in which a sufficient amount of time was spent on each determination to enable accurate threshold settings to be made.

Stimulation procedure. The fact that the threshold was observed more often to increase than to decrease may be taken as evidence

that the fluctuations were, at least to some extent, due to the stimulus procedure. The repeated deformation of a particular receptor may be suspected of causing a decrease in excitability during the course of an experiment. In fact, there was sometimes a marked rise in the threshold immediately after stimulation at high amplitude, especially if it was repeated at a high frequency—for instance, 100 per second. Apart from this, however, no relation could be established between the intensity of stimulation and the variations in threshold; sometimes the threshold remained constant or decreased during the course of an experiment with intense stimulation. Further, marked fluctuations were encountered in control experiments in which the stimulation was limited to single threshold determinations at long intervals of, for instance, a quarter of an hour.

Temperature. It has been shown that the temperature in the receptor region influences the excitability of certain mechanoreceptors in the skin (HOAGLAND 1933). The temperature variations encountered in the present experiments (p. 10) were, however, not parallel to the variations in threshold. Moreover, the threshold could be constant while the temperature varied, and *vice versa.*

Since the various experimental factors examined cannot be considered to account for the observed threshold fluctuations, it can be inferred that *the excitability in the receptors may vary with time.* These variations may be of a spontaneous, random nature or they may be guided by some internal process. The latter possibility will be further discussed below (p. 66), but one process that may conceivably be of this kind will be mentioned here, since it was the subject of experimental tests. As mentioned (p. 7), HABGOOD (1950) has found that stimulation of a cutaneous nerve may produce sensitization of sensory endings, among them mechanoreceptors, in the frog's skin. According to Habgood this sensitization is mediated by a substance that is released at the endings by antidromic impulses in thin afferents. In view of this it was considered to be of interest to examine whether *antidromic stimulation* of the tactile fibres under study might possibly induce threshold variations. This was the more justified since there was reason to suppose that their endings were subjected to antidromic

bombardment during adequate stimulation *(Chapter IV)*. Accordingly, the threshold was determined before and after antidromic stimulation of the dorsal root at such an intensity that the fibre studied was also stimulated. Antidromic stimulation at a frequency of 20 per second for periods up to 30 seconds was, however, not accompanied by any significant change in threshold when this was determined at one-minute intervals and comparisons were made with values obtained prior to antidromic stimulation.

3. Threshold of various receptors

Marked differences were observed between the thresholds for different receptors belonging to the same unit and between the mean thresholds for different units. For the great majority of sensitive points tested the threshold values were between 10 and 150 μ; some receptors required only a slight displacement—less than 10 μ. However, a certain displacement was always necessary to elicit a propagated impulse, and in no case was a spontaneous discharge observed. Some receptors required a greater displacement than 150 μ, and in one or two cases no response was obtained at 500 μ, the maximum amplitude available, although manual touch was an effective stimulation (*cf. Discussion*, p. 67).

Low-threshold receptors were found both distally and proximally on the leg. However, for units that were partly or wholly located on the digits—the apical units included—the thresholds were *on average* lower than for units located proximally. Since the skin on the digits is firmly attached to the underlying tissues, whereas the skin on the plantar surface and the calf is loosely attached and covers loose subcutaneous tissue, a series of tests was carried out to examine whether the threshold of a particular receptor was dependent on the compressibility of the underlying tissue. Variation of the compressibility was most easily effected for the web between the digits. It was found that the threshold value was lower when the skin rested on a firm base (cork) than when on a loose base (cotton). These results suggest that the lower values for the distal units may be due rather to the more efficient stimulation when the base is less compressible than to an inherent property of the digital receptors themselves.

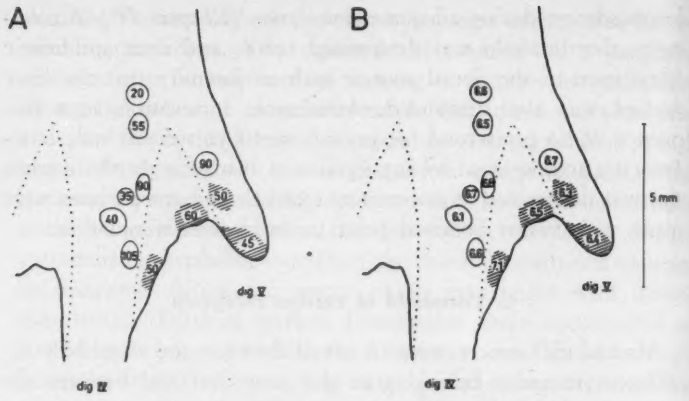

Fig. 10. Sketches of receptive field of tactile unit on plantar surface illustrating irregular distribution of threshold and latency. Sensitive warts are indicated by contours; sensitive points located on plain skin are hatched. Inset figures denote threshold in μ (*A*), and shortest latency in msec (*B*) for each receptor.

The threshold variations for receptors belonging to the same afferent fibre are illustrated in Fig. 10*A*, which shows a unit extending over the 4th and 5th digits and the web between them. Altogether, 11 sensitive points were found, the thresholds of which were between 20 and 105 μ. As appears from the figure, the distribution of various values throughout the field is irregular. In a series of 20 units the thresholds varied in the same irregular manner as for the unit in Fig. 10, although the percentage variation within any one unit was lower, especially in the case of those with few receptors.

When a high- and a low-threshold wart were close together, the impulse recorded on stimulation of the high-threshold wart might be suspected of being produced at the low-threshold wart through a spreading effect, since the displacement was extended at high stimulus amplitudes (*cf.* Fig. 3*B*). In such cases the stimulator was applied to the skin between the two warts or to an adjacent wart, manual stimulation of which did not result in a discharge in the fibre under study. For those "inactive" points where a response could be elicited at all by the maximum mechanical pulse a very high amplitude was required. These control experiments, as well as threshold determinations at adjacent warts (see *Methods*, p. 16), show that the mechanical stimulation was highly selective.

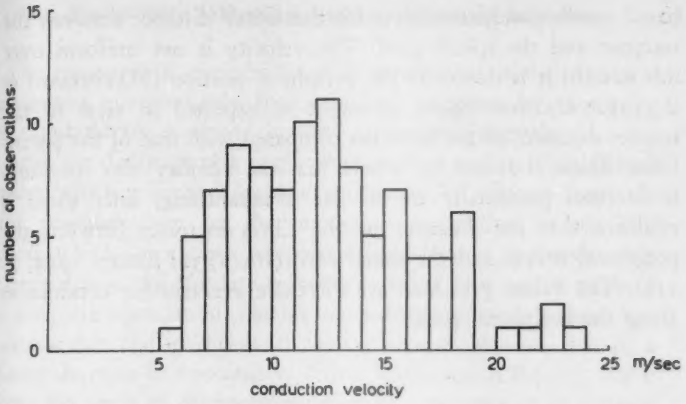

Fig. 11. Histogram. Mean conduction velocity from receptor to spinal cord for 97 tactile fibres.

4. Latency of the response elicited from various receptors

The shortest latency values obtained on supraliminal stimulation of various receptors belonging to the same unit differed slightly. A representative result is shown in Fig. 10*B*, in which the values for the shortest latency for each receptor of the unit have been inserted. There is a range of from 6.1 to 7.1 msec, the values being distributed irregularly within the field. The shortest latency values were not related to the thresholds (*cf.* Figs. 10*A* and *B*). A corresponding comparison for a number of units confirmed this finding.

The *conduction velocity* of the tactile fibres was calculated from the shortest latency value for the individual unit, measured from the time of maximum deformation and the length of the path from the stimulated receptor to the recording level in the dorsal root. From the histogram for 97 units (Fig. 11) it is seen that the calculated conduction velocity for most of the fibres was between 5 and 19 metres per second, and for a few between 20 and 24. The distribution was fairly uniform around the mean which was 12 metres per second.

The determinations of the conduction velocity made in this investigation differ from those performed earlier in that they are

based on the conduction time for the *whole* distance between the receptor and the spinal cord. The velocity is not uniform over this stretch; it is slower in the peripheral portion (MARUHASHI et al. 1952; CATTON 1958), as might be expected in view of the smaller diameter of the branches compared with that of the parent fibre. There is reason to believe that the velocity also continues to increase proximally to the site of branching, since there is evidence that the diameter of the fibres increases between the peripheral nerves and the spinal cord (IDE 1931; REXED 1944, p. 110). The values presented are therefore averages for conduction along the peripheral path.

CHAPTER III

1. Excitability following discharge of single impulses

The recovery of excitability after mechanical stimulation was determined quantitatively for individual receptors by measuring the threshold for a second impulse at various intervals.

After the discharge of a single impulse there was an initial period during which a second impulse could not be elicited from the same receptor even by the maximum mechanical pulse. This period, which for various receptors ranged from 3 to 6 msec, may be regarded as the *absolute refractory period* of a tactile receptor on adequate stimulation. During the subsequent period there was a measurable rise in threshold for the second impulse, that is, a *relative decrease in excitability*. This is illustrated in Fig. 12, which shows the result of double stimulation of a receptor at an interval of 15 msec. *A* and *C* are records from the dorsal root filament and

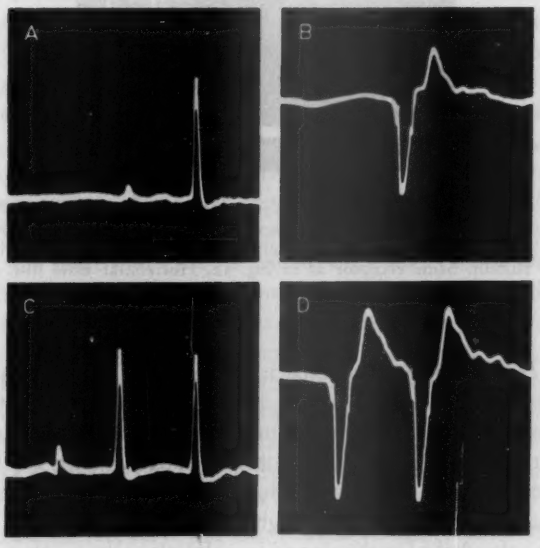

Fig. 12. Dorsal root fibre responses to single (*A*) and double (*C*) mechanical stimulation of apical touch unit, and records from capacitance meter showing threshold amplitude for initiation of the single impulse (*B*), and increase in threshold for the second impulse (righthand deflection in *D*). Horizontal scale line: 15 msec. Vertical scale line: 100 μ.

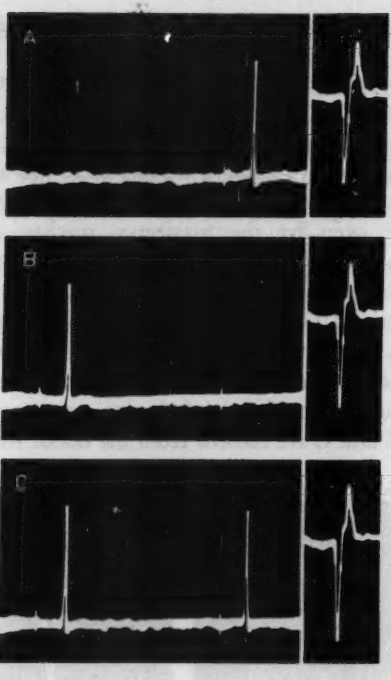

Fig. 13. Dorsal root fibre responses to single (*A*) and double (*B* and *C*) mechanical stimulation of tactile receptor illustrating decrease in excitability over a long interval. Capacitance records on the right give the amplitudes of the test stimuli. Same receptor as in Fig. 12. Horizontal scale line: 40 msec. Vertical scale line: 50 μ.

B and *D* the corresponding capacitance curves. The threshold for the discharge of a single impulse (*A*) was 80 μ (*B*). In *C*, the first impulse was elicited at supraliminal stimulus strength to ensure that it would appear at a constant latency when the test was repeated (*cf.* Fig. 8*D*), while the second impulse was elicited at threshold strength. From the righthand deflection in *D* it appears that the threshold for the second impulse was 120 μ—that is, 40 μ, or 50 per cent, greater than for the single impulse in *A*.

Fig. 13 shows the result when the same receptor as in Fig. 12 was stimulated at a longer interval (80 msec). The increase in

stimulus strength required for eliciting a second impulse (*C*) was in this case 10 μ—that is, 12 per cent above the unconditioned threshold value of 80 μ. A single impulse was thus followed by a decrease in excitability of *long duration*. In series of tests made on various receptors there was generally a measurable increase in the threshold value even after 200 msec. Stimulation at the unconditioned threshold value was sometimes ineffective for longer intervals—up to 300 msec—but the increase in stimulus strength that was required in order to obtain a second impulse was then too small to be measured accurately.

The course of the recovery of excitability was determined for each of a number of receptors and the result is illustrated in Fig. 14. The stimulus interval is represented by the abscissae, and the strength of the stimulus, expressed as the ratio of the threshold for the second and first impulses, by the ordinates. In the curve in *A* there is at first a steep decrease in the ratio as the stimulus interval is lengthened and then an asymptotic approach to the unconditioned value of unity. Analogous curves for a series of receptors belonging to different units showed a similar course although there were quantitative variations. This is also exemplified in Fig. 14, the two curves in which refer to different receptors. As in *A*, the curve in *B* falls steeply at first and then assumes an extended asymptotic course. A closer comparison shows, however, that the recovery is more rapid for the receptor in *B*. The difference is greatest for short intervals; for the 10 msec interval, for instance, the threshold was twice the unconditioned value for the receptor in *A*, whereas for that in *B* there was an increase of only slightly more than 30 per cent. Of the recovery curves for 40 receptors, all of which belonged to different units, some resembled the curve in Fig. 14*A* and others that in Fig. 14*B*, but the whole range of intermediate forms was also represented. As a consequence, the curves in Fig. 14 should be regarded as examples of quantitative variations rather than representing different types of receptors.

The rate of recovery was not related to the level of the unconditioned threshold or to the somatotopic location of the receptor. Both low- and high-threshold receptors displayed different rates of recovery; furthermore, different rates were encountered both for receptors on the digits and for those located more proximally.

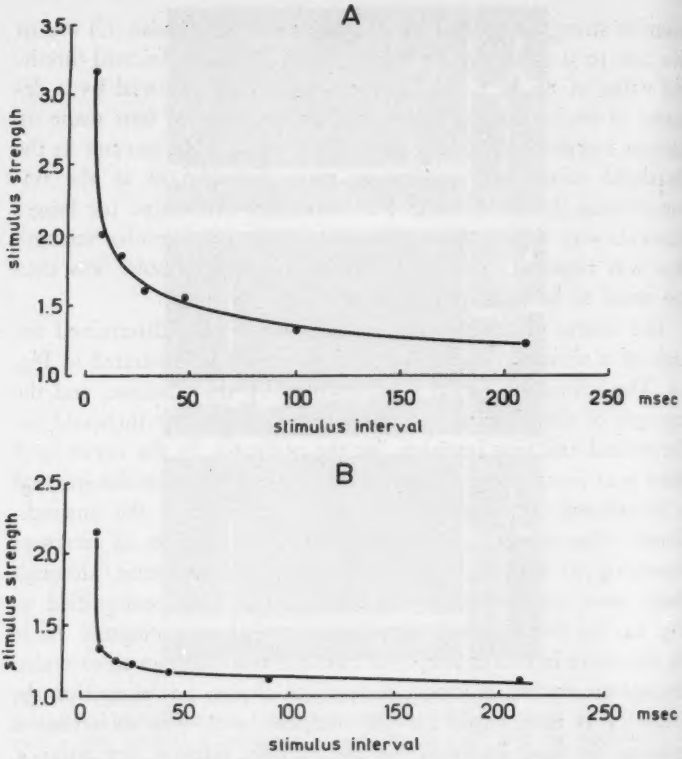

Fig. 14. Threshold time curves from two touch receptors illustrating recovery of excitability after initiation of a single impulse by mechanical stimulation. *Ordinates:* Stimulus strength necessary to elicit a second impulse, expressed as multiples of the unconditioned threshold value. *Abscissae:* Interval between conditioning and test stimuli. *A* from receptor belonging to unit on lower leg. Unconditioned threshold, 1.0 on ordinate scale, 80 μ. *B* from receptor belonging to another unit on lower leg. 1.0 = 75 μ.

The recovery curves in Fig. 14 are smooth, but for several receptors a deviation from the smooth form was observed, as is illustrated in Fig. 15. For the receptor represented by the curve in *A* there was a marked deviation; the threshold at 10 msec was only about 15 per cent higher than the unconditioned value, but it rose to slightly more than 170 per cent at the 15 msec interval.

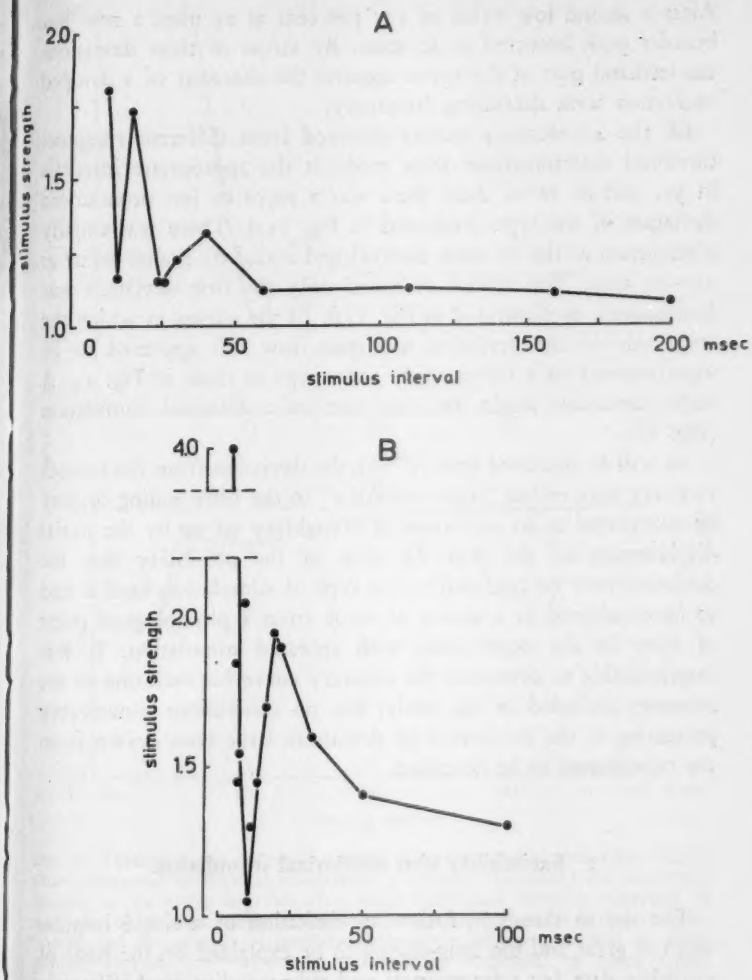

Fig. 15. Recovery curves showing deviations from the smooth course. Note increase in excitability at about 10 msec. Stimulation and plotting as in Fig. 14. *A* from receptor belonging to unit on distal plantar surface. 1.0 = 60 μ. *B* from receptor belonging to unit on lateral border of foot. 1.0 = 30 μ.

After a second low value of 115 per cent at 25 msec a new but broader peak occurred at 40 msec. By virtue of these deviations the lefthand part of the curve acquires the character of a damped oscillation with decreasing frequency.

Of the 40 recovery curves obtained from different receptors threshold determinations were made at the appropriate intervals in 30, and in 16 of these there was a more or less pronounced deviation of the type illustrated in Fig. 15*A*. There was usually a minimum at the 10 msec interval and a slightly higher value at 15—20 msec. For several receptors only the first deviation was conspicuous, as illustrated in Fig. 15*B*. In the curves in which the amplitude of the deviation was quite low this appeared to be superimposed on a curve of the same type as those in Fig. 14. A slight deviation might be seen also on *subliminal* stimulation (Fig. 16).

As will be discussed later (p. 70), the deviation from the smooth recovery may reflect "supernormality" in the fibre ending or may be interpreted as an oscillation in excitability set up by the initial displacement of the skin. In view of the possibility that the deviation may be confined to the type of stimulation used it had to be considered as a source of error from a physiological point of view in the experiments with repeated stimulation. It was impracticable to determine the recovery curve for each one of the receptors included in the study, but no conclusions conceivably pertaining to the occurrence of deviations have been drawn from the experiments to be described.

2. Excitability after subliminal stimulation

The rise in threshold following elicitation of a single impulse was too great and too long-lasting to be explained on the basis of available data for refractoriness and subnormality in A fibres in the frog as tested by electrical stimulation (see p. 68). To examine whether it might be due to a refractory state in the local events preceding the initiation of the propagated impulse the threshold was also tested after subliminal stimulation. It was assumed that a slightly subliminal stimulus would activate the receptor me-

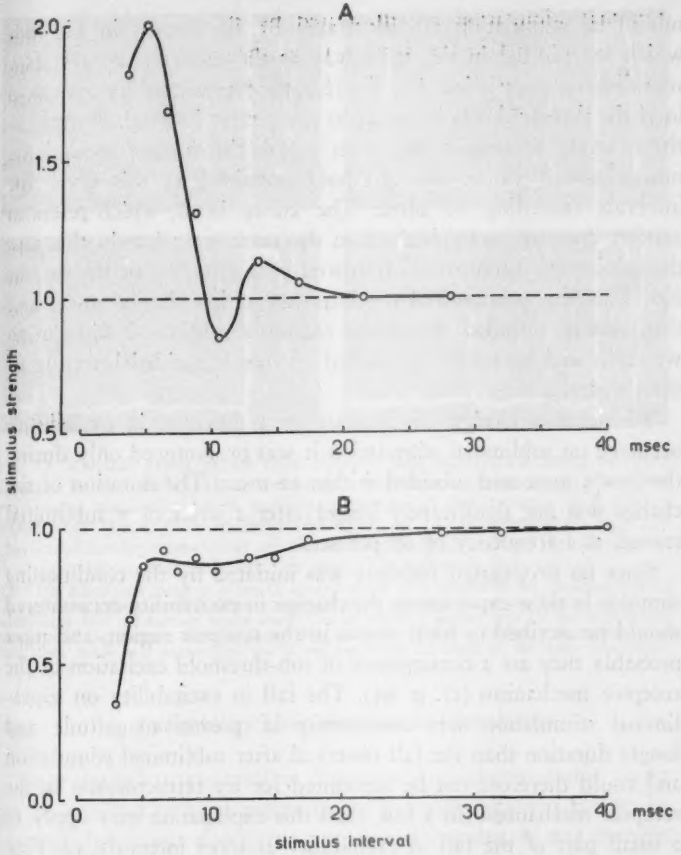

Fig. 16. Threshold time curves illustrating different types of excitability change after subliminal mechanical stimulation. *Ordinates:* Threshold for conducted impulse at successive intervals after single subliminal stimulus, expressed as multiples of the unconditioned threshold. *Abscissae:* Interval between conditioning and test stimuli. *A* from tactile receptor belonging to unit on distal plantar surface. 1.0 = 15—30 μ (fluctuating threshold). *B* from tactile receptor belonging to unit on lower leg. 1.0 = 140 μ.

chanism to almost the same extent as a threshold stimulus, the essential difference being that no propagated impulse would be generated.

The results of threshold determinations at various intervals after

subliminal stimulation are illustrated by the curves in Fig. 16, which are plotted in the same way as the recovery curves after supraliminal stimulation. For the receptor represented by the curve in *A* the threshold was increased at the 5 msec interval. Thereafter the recovery was rapid and, after a few fluctuations around the unconditioned value, the threshold remained at this level for intervals exceeding 20 msec. The curve in *B*, which refers to another receptor, was obtained in the same way, but in this case the subliminal stimulus was followed by a *lowering* of the threshold. This was pronounced for intervals of less than 5 msec, and then slowly subsided. For some receptors subliminal stimulation was followed by neither a decided rise nor a decided lowering of the threshold.

Whenever a change, an increase or a decrease, in excitability occurred on subliminal stimulation it was pronounced only during the first 5 msec and subsided within 20 msec. The duration of the change was not significantly longer after a series of 7 subliminal stimuli at a frequency of 68 per sec.

Since no propagated response was initiated by the conditioning stimulus in these experiments the changes in excitability encountered should be ascribed to local events in the receptor region, and most probably they are a consequence of sub-threshold excitation of the receptor mechanism (*cf.* p. 65). The fall in excitability on supraliminal stimulation was consistently of greater magnitude and longer duration than the fall observed after subliminal stimulation and could therefore not be accounted for by refractoriness in the receptor mechanism (in a few cases this explanation may apply to a small part of the fall in excitability at short intervals; *cf.* Figs. 14 and 16*A*). Moreover, the changes after subliminal stimulation diminished gradually when the strength of the conditioning stimulus was reduced, whereas the changes after supraliminal stimulation had the all-or-none character of the propagated impulses.

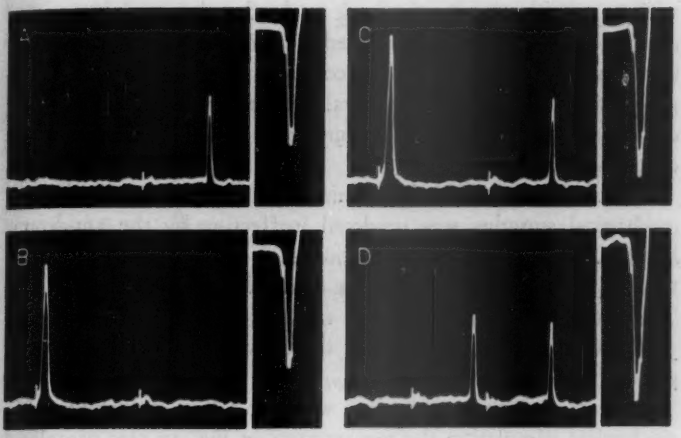

Fig. 17. Records from dorsal root filament and capacitance meter showing decrease in excitability after antidromic stimulation. Response to threshold mechanical stimulation in *A*, and disappearance of the response in *B* after a dorsal root shock. Rise in threshold after antidromic stimulation (*C*) and after conditioning stimulation of the test receptor (*D*). From apical unit on first digit. Horizontal scale line: 20 msec. Vertical scale line: 100 μ.

Note: The dorsal root shock in *B* and *C*, applied about 1 cm distally to the recording level, is followed by a spike potential, which is the part of the dorsal root response that was conducted centripetally into the filament under study. The amplitude is greater than for the orthodromic impulse since the filament contained more than one fibre of similar calibre. The strength of the dorsal root shock was adjusted so that it was just above threshold for the tactile fibre tested

3. Excitability after antidromic stimulation

Since the fall in excitability after supraliminal stimulation could not be ascribed to local events in the receptor region it had to be assumed that it was due to the propagated impulse. It was thought that direct evidence of this might be obtained with the aid of antidromic stimulation, since an antidromic impulse reaching that part of the fibre ending where the orthodromic impulse starts would cause a decrease in excitability for mechanical stimulation. A series of tests was performed, therefore, in which the threshold was measured at various intervals after antidromic stimulation of the dorsal root.

Such an experiment is illustrated in Fig. 17, where record *A* shows the response to the mechanical stimulation alone at threshold amplitude, 100 μ. In *B* a mechanical pulse of the same amplitude

was preceded by an electric shock to the dorsal root and no orthodromic impulse was then obtained, It should be pointed out that this could not be attributed to collision with the antidromic impulse, since the stimulus interval was 27 msec while the time calculated for the antidromic impulse to reach the periphery was only 7—8 msec.

The absence of an orthodromic impulse in *B* implies that the mechanical stimulus was rendered ineffective by the antidromic impulse. By increasing the amplitude of the mechanical stimulus to 135 μ an orthodromic impulse could, however, be elicited (*C*). This means that the excitability in the receptor was reduced by 35 per cent about 20 msec after the arrival of an antidromic impulse.

For a quantitative comparison with the fall in excitability after mechanical stimulation the test receptor in Fig. 17 was stimulated twice at an interval of 20 msec (Fig. 17*D*). The threshold for the second impulse was then 140 μ—that is, similar in magnitude to that after antidromic stimulation. Further, on varying the stimulus interval it was found that the recovery of a particular receptor displayed a similar course after antidromic and orthodromic stimulation. This is illustrated in Fig. 18, in which *A* shows the recovery curve after antidromic stimulation, and *B* (*filled circles*) that after orthodromic stimulation of the same receptor. To facilitate comparison the antidromic curve has been drawn in on the orthodromic one (*broken line*). The close agreement between the curves is evident.

The parallel between the course and magnitude of the fall in excitability following an antidromic and orthodromic impulse provides further and more direct evidence that the long decrease in excitability after supraliminal mechanical stimulation is associated with the propagated impulse.

4. Excitability following discharge of trains of impulses

Because of the long duration of the fall in excitability after a single impulse a certain degree of supraliminal stimulation was necessary to make the unit follow repeated stimulation even at low

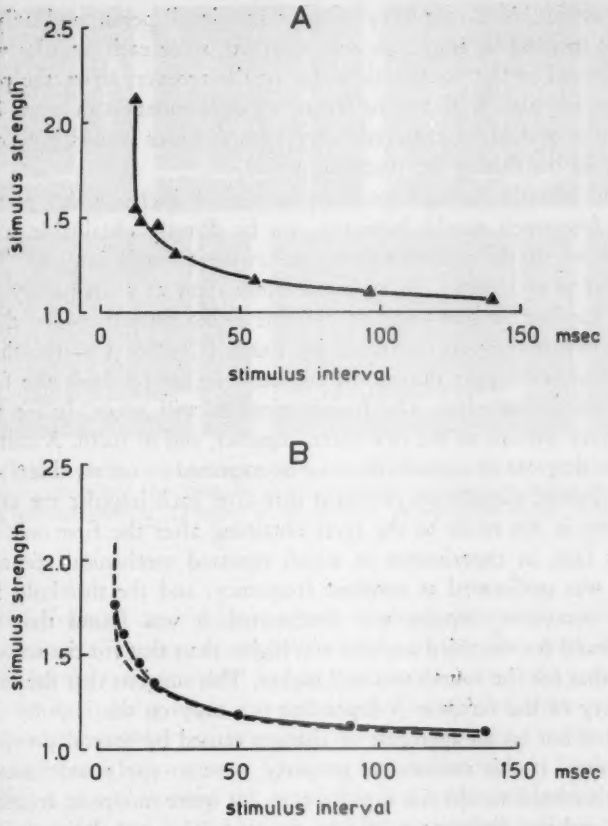

Fig. 18. Threshold time curves showing recovery excitability after antidromic stimulation (*A*) and supraliminal mechanical stimulation of the test receptor (*B, filled circles*). Stimulus strength expressed as multiples of unconditioned threshold amplitude, 100 μ. To facilitate comparison the curve in *A* has been entered as a broken line in *B* after reduction of stimulus interval by calculated conduction time for transmission of antidromic impulse to periphery. Same unit as in Fig. 17.

frequencies. At a frequency of 5 or 10 stimuli per second only a slight increase in amplitude was required, since each impulse was discharged in the asymptotic phase of the recovery after the preceding impulse. With a rising frequency of stimulation an increasing intensity would be required, since each stimulus occurs progressively earlier during the recovery period.

The stimulus strength necessary to elicit a discharge at a particular frequency would, however, not be directly obtainable from the level of the recovery curve following a single impulse. The reason is as follows. In repeated stimulation at a frequency of, say, 100 per second—not an extreme firing frequency for these units when they are activated by touch (*Chapter V*)—the third stimulus will occur during the recovery period for both the first and second impulses. The fourth stimulus will occur during the recovery periods of the first three impulses, and so forth. A cumulative decrease in excitability may be expected to occur, therefore, on repeated stimulation provided that after each impulse the excitability is not re-set to the level obtaining after the first one.

In fact, in experiments in which repeated mechanical stimulation was performed at constant frequency, and the threshold for each successive impulse was determined, it was found that the threshold for the third impulse was higher than that for the second, and that for the fourth was still higher. This suggests that the excitability of the receptor is dependent not only on the impulse just elicited but on an aggregate of changes caused by several previous impulses. If this cumulative property were to apply indefinitely, the threshold would rise rapidly even for quite moderate frequencies, and the discharge would be arrested. The cumulative fall in excitability might then be one of the reasons for the rapid adaptation displayed by these receptors following application of stimuli of longer duration. However, as in previous studies on intermittent mechanical stimulation arranged so as not to involve the adaptation process (Cattell and Hoagland 1931), it was found that the units could be made to follow fairly high frequencies for several seconds. This suggests that the total fall in excitability on repeated discharge of impulses is limited and can be offset by raising the strength of the stimulus. An accurate quantitative representation of the cumulative property and its limitation is exemplified in Fig. 19,

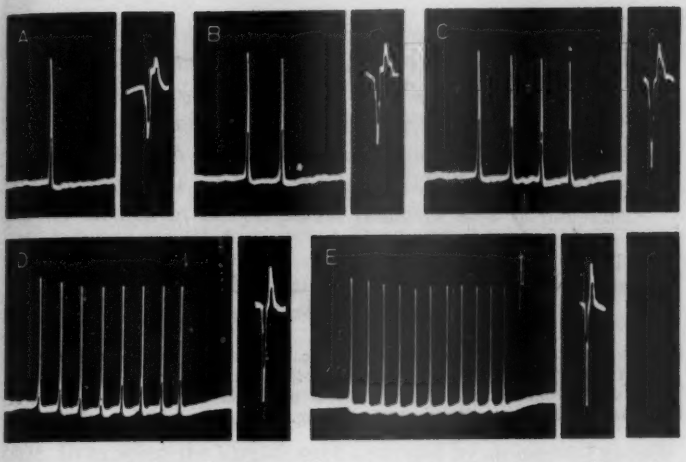

Fig. 19. Records from dorsal root filament and capacitance meter illustrating increasing threshold for initiation of impulses of progressively higher order. Same impulse interval (15 msec) in all records; sweep speed varies. Vertical scale line: 100 μ.

which is from an experiment in which the threshold was determined for successive impulses up to the eleventh; all impulses were elicited from the same receptor, and at a constant interval of 15 msec. The threshold for a single impulse was 50 μ (*A*). *B-E* show series of increasing numbers of impulses, and the threshold for the last impulse in each series appears from the capacitance curves. In order to elicit a second impulse the amplitude had to be increased from 50 to 65 μ (*B*) and for the fourth impulse an increase to 85 μ was required (*C*). The increase in threshold for the eighth impulse was less, 10 μ (*D*), and eleven impulses were obtained with an increment of only 5 μ to give a total of 100 μ (*E*). In Fig. 20 the thresholds are plotted as multiples of the value for the first impulse. It is seen that after the fourth impulse the increase in threshold reached a level of just below twice the unconditioned value, and the initiation of a greater number of impulses demanded a relatively small further increase in the amplitude. In a series of experiments of this type the increase in threshold levelled off at a ratio of between 1.5 and 4.0. Some units followed the tested frequency for several se-

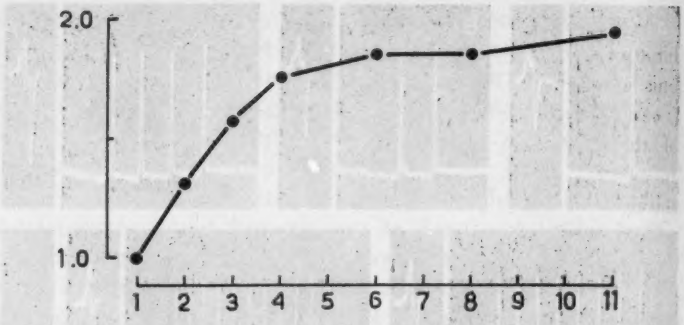

Fig. 20. Curve showing cumulative increase in threshold on repeated stimulation. *Abscissa:* Order of impulses from beginning of stimulation. *Ordinate:* Threshold strength expressed as multiples of the threshold for initiation of the first impulse. Same experiment as in Fig. 19.

conds after quite a small increment in stimulus strength above that ratio. In a few experiments the threshold rose to 500 μ—the maximum for the stimulator—without the curve levelling out. In the case of these receptors one cannot exclude the possibility of a further rise in threshold resulting in an appreciable reduction in the tendency for repeated discharge by virtue of the cumulative property.

The experiments on repeated stimulation thus show that the fall in excitability after successive impulses is cumulative; this counteracts repeated discharge from the stimulated receptor, though only to a limited extent. On increasing the amplitude of the stimulus by between 1.5 and 4 times the threshold value for a single impulse most of the receptors could be made to follow repeated stimulation with physiological frequencies.

CHAPTER IV

As mentioned above (*Introduction*, p. 5), evidence of an inhibitory interaction within the receptive area of a single peripheral unit was found by CATTELL and HOAGLAND (1931) and TOWER (1940). In the experiments to be described a quantitative study of the interaction between single receptors was performed and an evaluation was made of its significance for the integration of activity elicited in the peripheral branches of a tactile unit.

1. Excitability following discharge of single impulses in neighbouring receptors

When two receptors belonging to the same unit were stimulated simultaneously with separate stimulators at, or slightly above, their thresholds, only one impulse was recorded from the dorsal root fibre. Even when the stimuli were separated by an interval exceeding the refractory period for the afferent fibre, only one impulse was obtained; this was elicited from the receptor stimulated first. In Fig. 21, *A* shows the response to stimulation of a single receptor —which may be called the *test receptor*—at threshold amplitude (95 μ). From *B* it is seen that the strength of this stimulus was subliminal when an impulse was elicited 30 msec earlier from *another receptor* belonging to the same unit—such a receptor will in what follows be called a *neighbouring receptor*. Not until the amplitude of the test stimulus had been increased to 180 μ was a discharge obtained from the test receptor as well (*C*). A rise in threshold was also found when the conditioning and test stimuli were reversed, and when they were shifted in turn to the various other receptors belonging to the same unit. When a number of units were tested in the same way an increase in the threshold of the particular test receptor was consistently found.

There is thus a decrease in the excitability of the various receptors in a receptive field when one of them is stimulated at or above threshold for initiation of an impulse. From a functional aspect this means that all receptors belonging to the same unit exert an inhibitory action on one another.

Analogous conditioning experiments, in which the stimulus interval was varied, showed that the decrease in excitability at the various receptors of a unit following supraliminal stimulation of

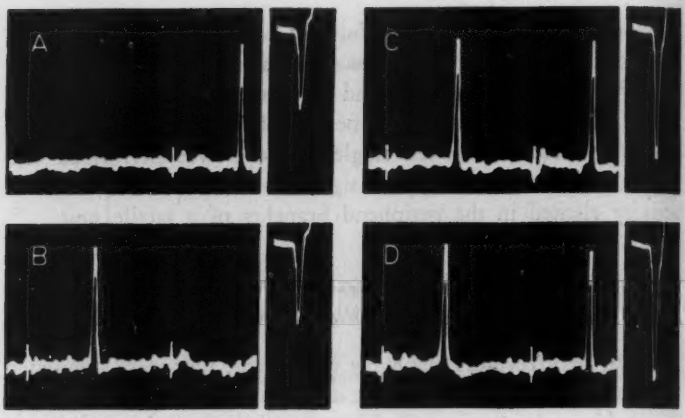

Fig. 21. Records from dorsal root filament and capacitance meter illustrating decrease in excitability on supraliminal mechanical stimulation of neighbouring receptor. *A:* Response to stimulation of test receptor alone at threshold amplitude. *B:* Absence of response to test stimulation of same strength as in *A* when an impulse has been elicited at another receptor of the unit 30 msec earlier. *C:* Rise in threshold of test receptor on conditioning stimulation as in *B*. *D:* Rise in threshold on conditioning stimulation of the test receptor itself 30 msec earlier. From unit on proximal plantar surface. Horizontal scale line: 20 msec. Vertical scale line: 100 μ.

one of them is of fairly long duration. The result of such an experiment is illustrated in Fig. 22. It is seen that an impulse could be elicited by strong supraliminal stimulation of the test receptor after a certain minimum interval (6 msec). When the stimulus interval was lengthened there was a gradual lowering of the threshold, but it was still slightly above the unconditioned value at 230 msec, the maximum interval tested. A series of curves was derived in the same manner as that in Fig. 22 for various pairs of receptors belonging to the same or different units. They all displayed a similar course, although quantitative variations occurred.

As the displacement caused by the mechanical pulses was local and of short duration (p. 14), the inhibitory interaction between the receptors could not be due to an extension of the displacement from the site of conditioning stimulation along the surface of the skin to the test receptor. As suggested already by CATTELL and HOAGLAND (1931), antidromic discharge in the peripheral branches is the most likely mechanism underlying the interaction. If each

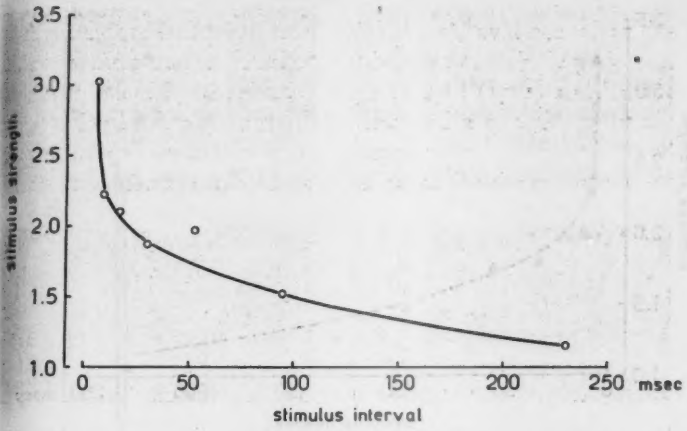

Fig. 22. Threshold time curve illustrating decrease in excitability on supraliminal mechanical stimulation of neighbouring receptor at zero interval. Same unit as in Fig. 21. Plotting as in Fig. 14. 1.0 = 80 — 115 μ (fluctuating threshold).

Note: The value for 50 msec interval lies outside the probable curve. The deviation in this case is probably due to erroneous setting of a supraliminal instead of the threshold value of the stimulus (*cf.* p. 25).

impulse initiated not only passes into the afferent fibre but also travels antidromically in the various peripheral branches of the fibre there will be a fall in the excitability of their endings (*cf. Chapter III:3*). If the interaction is to be explained along these lines the same recovery curve should be obtained on antidromic stimulation of the dorsal root fibre and on supraliminal stimulation of another receptor of the unit. In the experiment illustrated in Fig. 22 both types of stimulation were performed. The curve in this figure, which shows the recovery after supraliminal stimulation of a neighbouring receptor, has also been drawn in Fig. 23 (*broken line*). The rise in threshold for the same test receptor after antidromic stimulation (*filled triangles*) follows practically the same course. Consistent results were obtained when various receptors were similarly tested.

The close agreement between the recovery curves after antidromic stimulation of the afferent fibre in the dorsal root and supraliminal mechanical stimulation of a neighbouring receptor strongly indicates that the inhibitory interaction displayed by the

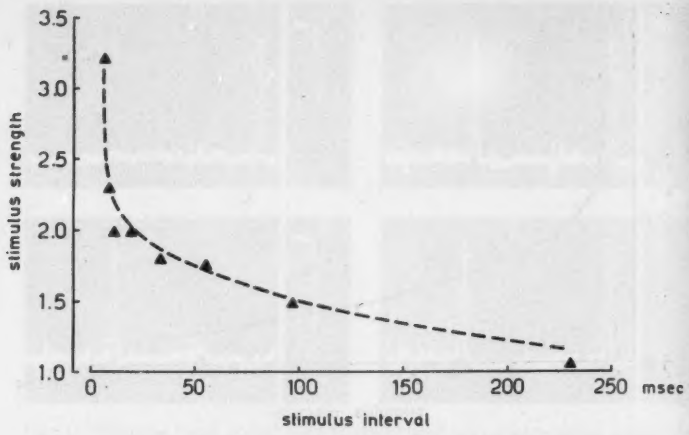

Fig. 23. Threshold time diagram showing parallel recovery of excitability after mechanical stimulation of neighbouring receptor (*broken line*, same curve as in Fig. 22) and after antidromic stimulation (*filled triangles*). For values obtained on antidromic stimulation the stimulus interval was reduced by 12 msec, the calculated period for conduction of antidromic impulses from dorsal root to receptor level. Same test receptor as in Figs. 21—2.

various receptors of a unit is a consequence of antidromic discharge in the peripheral branches of the afferent fibre.

It was pointed out by CATTELL and HOAGLAND (1931) that the peripheral interaction was dependent upon the initiation of propagated impulses by the conditioning stimulus. When adaptation of the receptors in one part of the receptive field was effected by the application of slowly rising pressure (air current) without any impulses being initiated, the duration of the discharge elicited from the rest of the field was unchanged. In the present study experiments were made in which the threshold of a single receptor was determined at various intervals after application of constant pressure or subliminal mechanical pulses to various other receptors belonging to the same unit. Such stimulation was not found to alter the threshold of the test receptor and did not influence the discharge in the afferent fibre. Experiments in which simultaneous subliminal stimulation of two receptors was performed were also negative in that no impulse was elicited in the afferent fibre; that is to say, subliminal stimuli were not additive.

These results indicate that subliminal changes in excitability and adaptation are local events, which do not spread beyond the particular branch of the afferent fibre whose end is activated.

In one series of experiments the increase in threshold on stimulation of a neighbouring receptor was compared with the increase on conditioning stimulation of the test receptor itself. The response

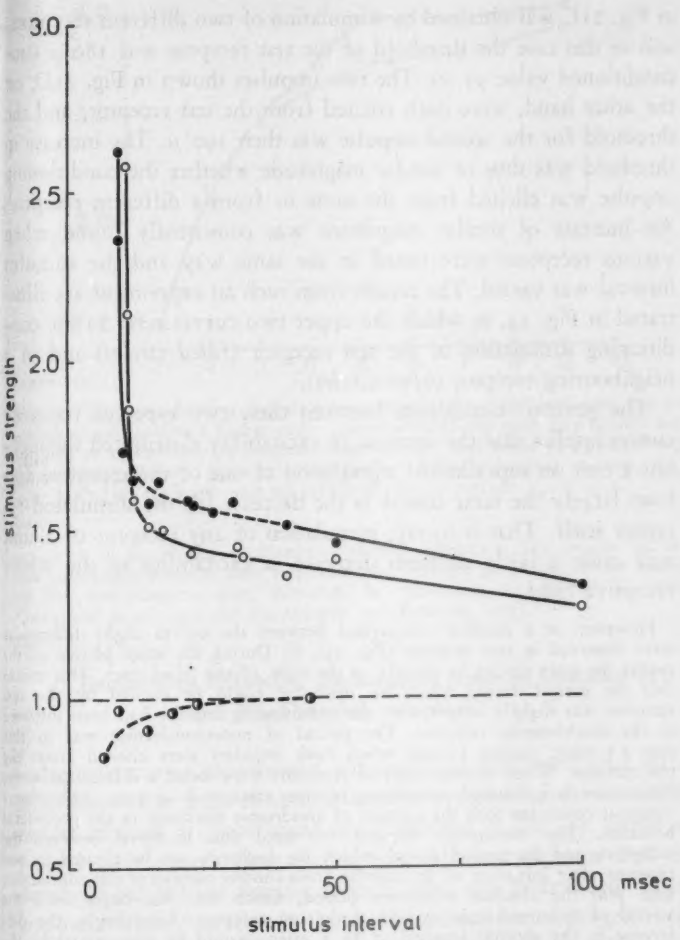

Fig. 24. Threshold time curves for comparison of recovery of excitability after supraliminal mechanical stimulation of neighbouring receptor (*open circles*) and of the test receptor (*filled circles*). *Half-filled circles* are thresholds after subliminal stimulation of the test receptor. Plotting as in previous recovery curves. From unit on proximal plantar surface. 1.0 = 115—170 μ (fluctuating threshold).

in Fig. 21*C* was obtained by stimulation of two different receptors, and in this case the threshold of the test receptor was 180 μ (unconditioned value 95 μ). The two impulses shown in Fig. 21*D*, on the other hand, were both elicited from the test receptor, and the threshold for the second impulse was then 190 μ. The increase in threshold was thus of similar magnitude whether the conditioning impulse was elicited from the same or from a different receptor. An increase of similar magnitude was consistently found when various receptors were tested in the same way and the stimulus interval was varied. The results from such an experiment are illustrated in Fig. 24, in which the upper two curves refer to the conditioning stimulation of the test receptor (*filled circles*) and of a neighbouring receptor (*open circles*).

The general resemblance between these two types of recovery curves implies that the decrease in excitability distributed throughout a unit on supraliminal stimulation of one of the receptors follows largely the same course as the decrease for the stimulated receptor itself. That is to say, stimulation of any receptor of a unit will cause a fairly uniform decrease in excitability in the whole receptive field.

However, in a detailed comparison between the curves slight differences were observed in two respects (Fig. 24). (i) During the steep phases of the curves the open circles lie slightly to the right of the filled ones. This means that the period during which no discharge could be elicited by the test stimulus was slightly longer after the conditioning impulse had been initiated in the neighbouring receptor. The period of unresponsiveness was in this case 7.5 msec, against 6 msec when both impulses were elicited from the test receptor. When various pairs of receptors were tested a difference in the same sense was obtained, amounting in most cases to 1—2 msec. This observation is consistent with the concept of antidromic discharge in the peripheral branches. The antidromic impulse will need time to travel between the receptors, and the period during which no discharge can be elicited in one receptor after initiation of an impulse from another consists of this conduction time *plus* the absolute refractory period, which does not begin until the arrival of the antidromic impulse at the test receptor. Accordingly, the difference in the shortest interval—1 to 2 msec—would be approximately the time required for conduction between two receptors.

(ii) The second difference between the two types of curves was observed in their nearly horizontal portions. As seen in Fig. 24, the increase in threshold was slightly smaller after stimulation of the neighbouring receptor (*open circles*). The threshold values obtained after *subliminal* stimulation of the test receptor are also shown in the figure (*half-filled circles*), the effect on the excitability being of short duration and consisting chiefly of an increase (*cf.* Fig. 16*B*). The slightly higher threshold after conditioning stimulation of the test receptor (*filled circles*) can thus hardly be ascribed to a summation with refractoriness in the receptor mechanism (*cf.* p. 38). There

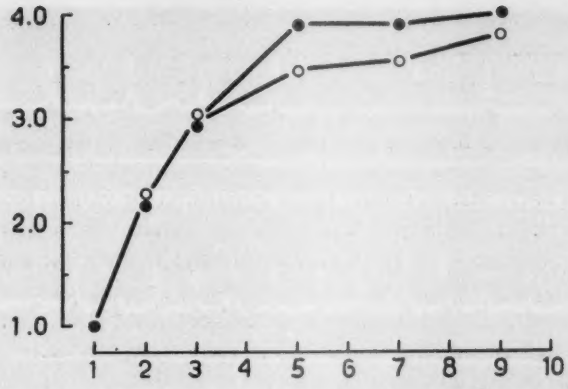

Fig. 25. Diagram showing cumulative increase in threshold (*ordinate*) for impulses of progressively higher order (*abscissa*) when the preceding stimuli were applied to a neighbouring receptor (*open circles*), and when all impulses were elicited from the test receptor (*filled circles*). Impulse interval 10 msec. Plotting as in Fig. 20. From unit on proximal plantar surface. 1.0 = 45 μ.

seems to be no obvious explanation of this difference. The possibility that the antidromic impulse does not reach the extreme periphery of the ending of the test receptor may, however, be taken into account (*cf.* Diamond, Gray and Sato 1956 and Eyzaguirre and Kuffler 1955).

2. Excitability following discharge of trains of impulses in neighbouring receptors

In one series of experiments, the threshold was tested after trains of impulses had been elicited at another receptor of the unit. The results of such an experiment are illustrated in Fig. 25. Series of 2—9 impulses were first elicited from the test receptor and the threshold for the last impulse in each series was determined. There was a cumulative increase in threshold for impulses of progressively higher order (*filled circles*), as described above (p. 43, Fig. 20). Only the last impulse in each series was then elicited from the test receptor, while the preceding impulses were evoked by stimulation of a neighbouring receptor. A similar cumulative increase in threshold was found in this case (*open circles*).

The result implies that the decrease in excitability distributed to the various receptors of a unit on supraliminal stimulation of one

of them is cumulative during repeated stimulation, as is the decrease in the stimulated receptor itself.

3. Integrated response to repeated stimulation of two receptors

It is likely that on natural touch stimulation the various receptors of a unit will be subjected to stimuli of different strength which, if the receptors were activated individually, would elicit different frequencies in the afferent fibre. However, owing to the topographic arrangement in which several receptors are close together, a natural touch stimulus will involve several receptors more or less simultaneously. The resulting response in the afferent fibre will then be determined by how the responses from the various receptors are integrated. In order to study the peripheral integration, model experiments were arranged in which repeated stimuli were applied simultaneously to two receptors belonging to the same unit.

In one series of experiments two receptors were stimulated at different frequencies. In Fig. 26, record *A* shows a train of impulses elicited by stimulation of one receptor at a frequency of 32 per sec, and *B* a train from a neighbouring receptor stimulated at 68 per sec. For each receptor the amplitude of the stimuli was set at the threshold value for that particular frequency (*Chapter III:4*). Record *C* shows the result when the two receptors were stimulated simultaneously. The frequency is the same as in *B;* that is, the same as for the discharge from the receptor stimulated at the *higher* frequency. By measuring the latency of the individual impulses in relation to the stimuli (*lower traces*) it could for nearly all impulses be decided from which receptor they were derived, and it was found that they originated from the receptor in *B*.

In the cases of coincident markings, as for one or two impulses in the first part of record *C*, latency measurements were not decisive. There is, however, another circumstance that makes it improbable that any impulse in *C* is derived from the receptor in *A*, which was stimulated at the lower frequency; the last stimulus to this receptor (*cf.* lower traces in *A* and *C*) was ineffective, although the interval between this and the preceding stimulus (see lower trace in *C*) was at least as long as any earlier interval in the series.

The results of this and similar experiments indicate that when two receptors, which on separate stimulation initiate different

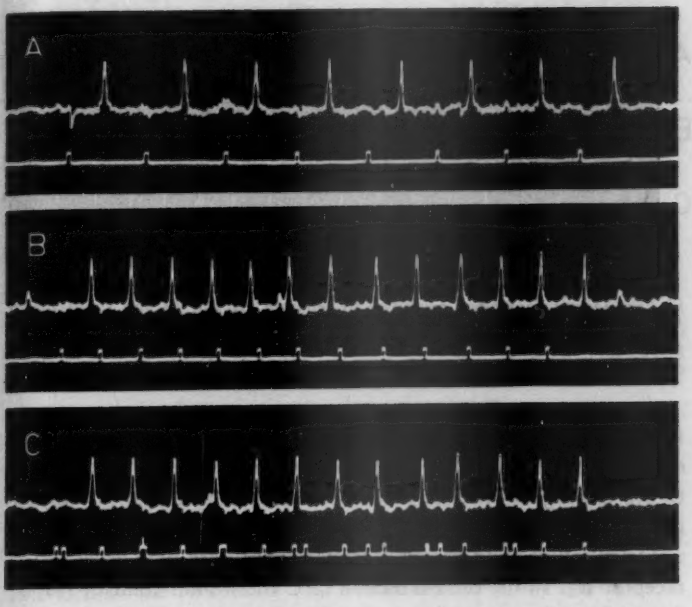

Fig. 26. Dorsal root fibre responses (*upper traces*) to separate (*A* and *B*) and simultaneous (*C*) repeated stimulation of two receptors belonging to unit on distal plantar surface. Trains of stimuli of different frequencies applied to each receptor, 32 per sec in *A*, 68 per sec in *B*. Generator pulses shown in *lower traces;* pulses in *C* corresponding to those in *A* and *B*, respectively, are found along the same vertical line.

impulse frequencies, are stimulated simultaneously, only the impulses from the receptor discharging at the higher frequency will enter the afferent fibre.

In order to elucidate the situation obtaining when different receptors are subjected to touch stimuli of similar intensity another series of experiments was performed, in which two receptors were stimulated at approximately the same frequency. The results are illustrated in Fig. 27, in which *A* and *B* show the responses to separate stimulation of two receptors, R_A and R_B, respectively, and *C* shows the response to simultaneous stimulation of both receptors. It appears that the impulse frequency in the afferent fibre is the same in *C* as for the separate stimulations, about 40 per sec. By

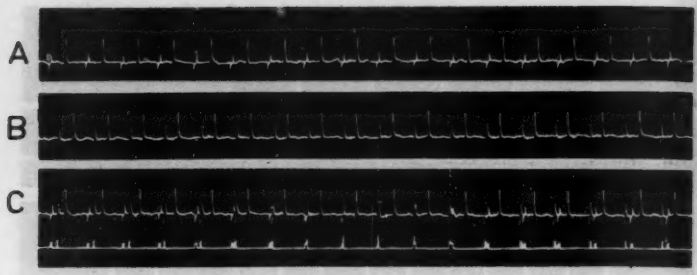

Fig. 27. Dorsal root fibre responses to separate (*A* and *B*) and simultaneous (*C*) repeated stimulation of two receptors belonging to unit on proximal plantar surface. Both receptors were stimulated at nearly identical frequencies of about 40 per sec and at threshold strength for this frequency.

means of latency measurements most of the impulses in *C* can be referred to the respective receptors; the artefacts that mark pulses to R_B are higher than those from stimulation of R_A. At the beginning of the simultaneous stimulation the impulses appear at the right time in relation to small artefacts; they are here generated in receptor R_A. In the central section of *C* the stimuli coincide (superimposed artefacts), so that it is impossible to decide from which receptor the impulses were derived. To the right in record *C* the stimuli have been displaced in phase and the larger artefacts are just in advance of the smaller ones; the impulses in this part of the record are related to the larger artefacts, which means that their origin has shifted to receptor R_B.

From this and analogous experiments it can be concluded that when two receptors belonging to the same unit are stimulated simultaneously at approximately the same frequency, only impulses from one of the receptors at a time will be transmitted into the afferent fibre. The impulse frequency will not exceed that for separate stimulation of each receptor.

CHAPTER V

In the foregoing chapters the excitability and the integration of the response in single tactile units were analysed with the aid of short mechanical pulses. To ascertain the significance of the results with respect to natural stimulation the responses to manual touch were also studied. A manual tactile stimulus has a different wave form and involves several factors, for instance adaptation, that do not apply when short pulses are used.

1. Manual tactile stimulation of single receptors

The manual touch stimuli could be localized to single sensitive points by using a small blunt needle. The amplitude and the speed of the manual stimuli were adjusted for each receptor so as to give a large total number of impulses per stimulation.

When a particular receptor was touched repeatedly the motion was as far as possible reproduced to provide a uniform stimulus. Nevertheless, in a series of bursts of impulses elicited from a single receptor, considerable variations in duration and impulse frequency of the discharge were encountered. The variations are illustrated in the records in Fig. 28, which show the responses to three cases of manual tactile stimulation applied to the same receptor at intervals of a few seconds. The irregular spacing of the impulses within each burst is probably a consequence of small variations in the skin displacement during the course of the individual stimulation.

For each burst the duration and mean impulse frequency were determined, and the maximum frequency was calculated from the shortest recorded interval between two impulses. For a large number of receptors the duration of the discharge ranged from about 50 to about 300 msec. The mean frequency was between

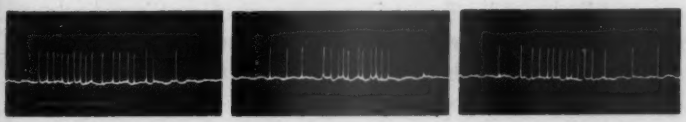

Fig. 28. Dorsal root fibre responses to three consecutive manual tactile stimulations of single receptor, repeated at intervals of a few seconds. From unit on proximal plantar surface. Scale line: 100 msec.

50 and 150 impulses per second, values around 90 being the most common, and the maximum frequency was generally between 180 and 300 impulses per second. The figures for the maximum frequency are compatible with the length of the absolute refractory period of the receptors, 3—6 msec, as determined with the mechanical stimulator (p. 31). Further, they are of the same magnitude as those obtained by previous authors following stimulation of the whole or the greater part of the receptive field (see *e.g.* ADRIAN et al. 1931).

On account of the variations in duration and frequency observed when the stimulation was repeated the mean values for a number of consecutive bursts, usually 10, were calculated for each receptor to enable a comparison between the discharges from different receptors to be made. The extent of the variations displayed by series of consecutive bursts is exemplified in the table below, in which the two upper rows show the extreme and mean values from 10 consecutive stimulations of two receptors, R_1 and R_2, respectively. (R_1 is the receptor the discharge of which is illustrated in Fig. 28.)

The average mean and maximum impulse frequency was often not of the same range for various receptors belonging to the same unit, and sometimes considerable differences were found. The conclusion would be the same as that reached on the basis of the experiments in which the threshold for initiation of single impulses was determined, namely, that neighbouring receptors may differ in excitability (*cf.* p. 67). Further, in these tests, the duration of the discharge might vary appreciably from one receptor to another, even when the stimuli were of similar intensity. Differences in duration were also observed on applying maintained pressure instead of touch; this suggests that the adaptation time varies within the receptive field. The differences in duration and impulse frequency displayed by the various receptors of a unit were apparently not related to their position within the field; this would be compatible with the above random distribution of thresholds (p. 28, Fig. 10*A*).

2. Integrated response to manual tactile stimulation of two or more receptors

In a series of experiments a comparison was made of the responses obtained on separate and simultaneous touch of two receptors belonging to the same unit. The values given in the adjoining table were obtained in such an experiment (each set of values represents 10 consecutive bursts). Stimulation of receptor R_2

	duration msec			mean frequency imp/sec			maximum frequency imp/sec		
	min.	mean	max.	min.	mean	max.	min.	mean	max.
R_1	90	*160*	215	65	*92*	110	140	*165*	230
R_2	150	*210*	300	70	*87*	110	135	*185*	250
$R_1 + R_2$	170	*225*	280	85	*99*	120	140	*183*	230

(*middle row*) resulted in bursts of longer duration and slightly higher maximum frequency but with a mean frequency that was similar to that of the discharge from receptor R_1 (*upper row*).

The values in the lower row were obtained on simultaneous touch of R_1 and R_2 and they closely resemble the values obtained on separate stimulation, especially those for R_2. Similar experiments performed on other units gave largely the same results, that is, the values obtained on simultaneous stimulation of two receptors were practically identical with, or at least did not appreciably exceed, those for stimulation of one of the receptors alone. When, on individual stimulation of the receptors, different values were obtained, the values for simultaneous stimulation resembled those for the receptor whose discharge had the higher frequency and the longer duration.

The results of the experiments with manual stimulation thus indicate that if two receptors are touched simultaneously the impulse frequency in the afferent fibre will not exceed that generated by one of the receptors on individual stimulation. Since different values for frequency and duration might be found for the various receptors of a unit, the integrated discharge when two or more receptors are stimulated simultaneously may differ to some extent from the discharge obtained by stimulation of only one receptor, depending upon which receptors are stimulated. There

will, however, be at least one receptor in each receptive field that is capable alone of giving a discharge as powerful as that obtained on simultaneous stimulation of all the receptors.

The fact that several receptors may be connected to a single fibre may, under certain conditions, imply that the discharge differs from that which would be obtained if the fibre were supplied with only one receptor. This was found in experiments on units having fairly *large* receptive fields and when a *tangential* stimulus was allowed to move over the field at the *appropriate speed*. In these experiments a series of strokes was first applied to the skin with intact receptive field. All but one of the sensitive warts were then inactivated by pinching with forceps, and the stimulus procedure was repeated. The mean duration was shorter and the mean frequency lower for series of bursts obtained after pinching when only one receptor discharged the fibre. The longer duration of the original response may be ascribed to the fact that the unit was stimulated for a period equal to the sum of the duration of the stimulus and the time it took for it to travel from one boundary of the field to the other. The higher mean frequency may be due to the gradual involvement of new receptors activated in succession by the most effective part of the stimulus. It should be pointed out that, owing to the variations encountered within each series, the range of values obtained before and after pinching, respectively, overlapped. Further, it could not be ascertained in these experiments whether the differences between the averages in the two series were greater than the differences which may be obtained on individual stimulation of neighbouring receptors.

3. Wave form of manual tactile stimulus

The wide range of the values for frequency and duration displayed by a series of bursts elicited by manual touch of a single receptor suggested that the individual stimuli varied considerably. In order to obtain an idea of the wave form of a manual touch stimulus and its variations in the actual experiments, the transducer of the capacitance meter was inserted under a wart on a piece of toad skin mounted on a perspex plate. The capacitance changes produced by the types of manual stimuli used were recorded and photographed, and the results are illustrated in Fig. 29*A*—*C*. Fig. 29*D* shows the traces from 10 consecutive touch stimulations. As seen, the gradient, the amplitude and the duration all vary. It is likely that these

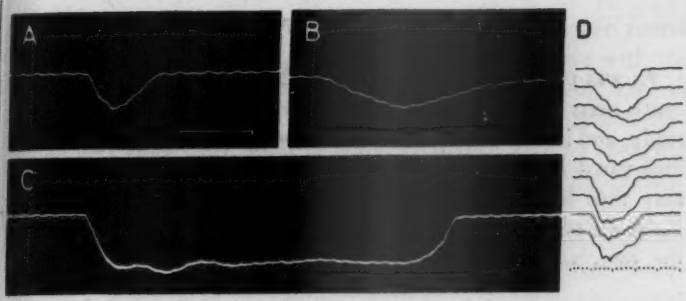

Fig. 29. Capacitance records showing vertical displacement at single wart following touch (*A*), stroking with a camelhair brush (*B*), and pressure (*C*). Scale line in *A:* 100 msec; same time scale in *B* and *C*. *D* shows the traces from 10 consecutive stimulations by touch; time in 10 msec. The superimposed 50-cycle ripple is due to the power supply of the capacitance meter.

variations of the stimulus are largely responsible for the variations displayed by the impulse discharge elicited by manual stimulation of a particular receptor. It should be pointed out that a direct comparison such as that between the impulse frequency of the discharge and the gradient of the stimulus cannot be made on the basis of the capacitance records in Fig. 29, primarily because these represent only the vertical deformation. An unknown part of the excitatory effect on the receptor will be due to lateral displacement of the skin.

In spite of the fact that the manual stimuli used were poorly standardized from the point of view of the displacement of the skin and the form of the discharge in the afferent fibre, most stimuli in a series were *felt* as being identically reproduced when applied to the back of the *human* hand. This may mean that variations displayed by the discharges in a particular peripheral unit are smoothed out in the central nervous system. The central (sensory) effect is probably determined by the discharge in a number of afferent fibres and variations of the unit discharge may then be of comparatively little importance (*cf. Intensity discrimination*, p. 72).

CHAPTER VI

Excitability in overlapping units

As was pointed out by ADRIAN et al. (1931) the fields of single touch units overlap extensively. This was confirmed in the present study, and it was found that one sensitive point or wart was usually innervated by several units. Endings belonging to different units may thus lie close together, and the question arose whether the initiation of impulses in such endings may be linked. This may be the case, according to evidence obtained by MATTHEWS (1929) on skin-nerve-muscle preparations from the frog. Impulses having twice the amplitude of a single impulse were frequently observed in the discharge elicited by mechanical stimulation of the skin, or by muscular stretch, and these "double" responses were thought to be due to two end-organs being synchronized. In the present investigation the possibility of an interaction between different *units* was studied in three types of experiments performed on occasions when two tactile fibres with overlapping receptive fields were contained in the same dorsal root filament (Fig. 30). The first two experiments to be described are concerned with the initiation of impulses.

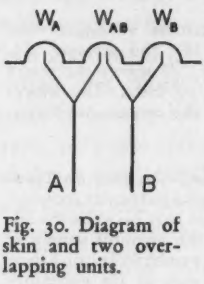

Fig. 30. Diagram of skin and two overlapping units.

(i) When a wart innervated by both units, such as W_{AB} in Fig. 30, was stimulated mechanically, the responses of the two units, *A* and *B*, had separate thresholds, and the latencies were usually different. The shortening of the latencies on increasing the stimulus strength occurred independently for the responses of the two units. Thus, impulses may be initiated in adjacent endings without evidence of interaction.

(ii) As indicated by the results described previously (*Chapter IV: 1)* a discharge of impulses elicited by mechanical stimulation at one sensitive point is conducted antidromically to other endings in the same receptive field. On the assumption that such a discharge might influence the excitability in endings belonging to overlapping units the following type of test was made. Single or repeated impulses were elicited from a wart innervated separately, for example W_A in Fig. 30, and the thresholds were determined at

a wart innervated by both units, such as W_{AB}. It was then found that the threshold for unit *A* rose, which is in accordance with the distribution of the increase in threshold throughout a field, whereas the threshold for unit *B* was unchanged. Hence, an antidromic discharge may apparently occur in one fibre branch without changing the excitability in a closely adjacent, probably interlocking ending, such as, in this case, that belonging to unit *B*.

(iii) An interaction might be expected to occur in overlapping units because of the hypothetical proximity of the afferent fibres, especially when these are contained in the same dorsal root filament. As shown by KATZ and SCHMITT (1940), subliminal changes in excitability occur in one fibre during impulse propagation in an adjacent fibre, and a mutual interaction, leading to alterations of conduction velocity, takes place when impulses are elicited simultaneously in both fibres. In the present investigation the shortest latencies of the responses obtained in filaments with overlapping units were measured, and the values for separate and simultaneous stimulation of the units were compared. This was done for five of the filaments only, but for none of these could an interaction be ascertained. One of the experiments is illustrated in Fig. 31, where records *A* and *B* refer to individual mechanical stimulation of two warts having separate innervation, such as W_A and W_B in Fig. 30, each at a supraliminal stimulus strength. The unit with the larger spike (*B*) displayed shorter latency, indicating a higher conduction velocity for the afferent fibre of this unit. Records *C*—*H* show the results of stimulation of the two units with small displacements in time. An interaction would presumably be manifested as a change in latency — for instance, a shortening of the latency for the unit with the lower conduction velocity (*cf.* KATZ and SCHMITT 1940). However, the latencies of the two impulses remained the same for all the combinations of stimuli. An interesting feature is observed in record *E*, where the larger impulse, though probably initiated later (right square-wave pulse on time scale), caught up and passed the slower impulse, this occurring without any visible influence on the transmission of the latter impulse. The same thing is seen in *F* and *G*, the only difference being that the initiation of the faster impulse has been further delayed. In record *H* the spikes appear to be synchronized,

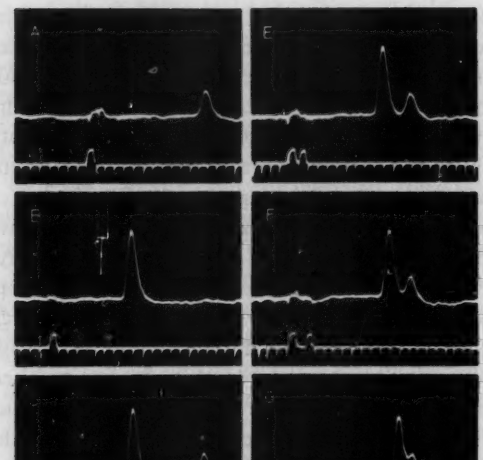

Fig. 31. Dorsal root fibre responses from two overlapping units showing independent impulse transmission. Time: 1 and 5 msec.

but a closer inspection shows that the stimulus interval was such that they should coincide at the recording level.

From the experiments with overlapping units it is inferred that peripheral tactile neurons, even when closely related anatomically, may function independently. The results imply that an interaction is not bound to occur, but because of the limited number of experiments it cannot be stated that it never takes place when there is adequate stimulation, and the lack of evidence of interaction in these experiments does not invalidate MATTHEWS' (1929) interpretation of "double" responses.

DISCUSSION

Validity of observations. The decerebrate preparation was preferred to the isolated nerve-skin preparation, primarily because it was believed that the chemical environment of the receptors would be constant (*cf.* p. 7). The condition of the animals was checked by means of general tests of the reflex excitability and by observing the circulation in the spinal vessels. However, the results may have been influenced by the experimental procedures, such as narcosis and laminectomy.

It should be borne in mind that the units were chosen with respect to their accessibility for stimulation with the mechanical stimulator and that a selection of fibres was probably involved in the dissection of the dorsal root. These two factors, among others, may have influenced the frequency of the observed phenomena.

Field size. Variations in the area of skin innervated by a single fibre were observed in all regions examined on the hindleg; on average, the receptive fields were smaller distally, however. This may be a manifestation of a general principle that the field area diminishes gradually in a distal direction, as may also be the fact that the fields found by ADRIAN et al. (1931) on the trunk of the frog appear to have been larger than the average for the present study. YAMAMOTO, SUGIHARA and KURU (1956) observed a corresponding variation of the field area on the hindleg of the cat. The functional significance of the size of the receptive field is dealt with in the discussion on discriminative sensibility (p. 74).

Branching. To some extent at least, the peripheral branching of the coarse sensory fibres studied occurs near, if not actually in, the skin (for references, see p. 9). There is, however, evidence that branches may be given off more proximally, as is common in the case of small afferents (see RANSON, DROEGEMUELLER, DAVENPORT and FISHER 1934, p. 18). DUNN (1909) has shown that splitting of afferent medullated fibres innervating the leg of the frog occurs in both the thigh and the shank, and ADRIAN

et al. (1931) found that tactile fibres in the frog may ramify even at the level of the dorsal root ganglion. ADRIAN et al. (1931) also found that a single tactile fibre may innervate widely separated areas of the trunk skin. This is probably associated with the proximal branching. In the present study, in which recording was made at the dorsal root level, the receptors belonging to a particular unit were never more than a few millimetres apart. This suggests that the touch units in the hindleg of the toad rarely, if ever, branch proximally. In fact, there appears to be direct evidence that these units generally ramify distally. As the area of the receptive fields is similar in size to that found by MARUHASHI et al. (1952), who recorded at the entrance of the *N. tibialis* into the *N. ischiadicus*, it would seem that the branching occurs peripherally to that level. Furthermore, the calculated time of 1—2 msec for conduction between two receptors (p. 50) is an indication of distal branching provided there are no transverse connections between the branches at the level of the skin; this interval is too short to allow transmission of the impulse by way of branches given off remote from the skin.

Conduction velocity. The conclusion to be drawn from the velocity determinations (Fig. 11) is that the tactile discharges were conducted in A fibres with a fairly wide range of calibre. This is consistent with HARRIS's (1935) results obtained on the frog by means of an indirect method. Tactile fibres conducting at a higher velocity, up to 35 m/sec, were encountered in the toad by MARUHASHI et al. (1952), and a faster range was found by CATTON (1958) for units in the frog's skin, which according to his classification are nearest the type studied here.

The velocity range found in the present investigation is similar to that for A fibres in skin nerves of the bullfrog (ERLANGER and GASSER 1930). Further, the units studied cover the same range as the fastest fibres found on electrical stimulation of various small skin nerves in the frog (BLAIR and ERLANGER 1933, p. 561). Beta, gamma and possibly also delta fibres may be engaged, although the histogram gave no indication of a subdivision. There was only one peak, at the mean velocity, 12 m/sec, and the distribution was fairly uniform. It should be pointed out that the relationship between the fibres studied and the elevations of the

compound action potential from a peripheral nerve or dorsal root, such as those obtained from the sciatic nerve of the bullfrog (ERLANGER and GASSER 1924, 1927), cannot be determined exactly. The main reason for this is that the present values for the conduction velocity are averages for the whole peripheral path (p. 30).

One source of error in the velocity determinations is the uncertainty as to the precise moment when the impulse starts. For the pacinian corpuscle of the cat, which is also a low-threshold mechanoreceptor, the minimum delay between the onset of the deformation and the initiation of the impulse is known to be about 0.5 msec (GRAY and MALCOLM 1950; ALVAREZ-BUYLLA and DE ARELLANO 1953; *cf.* GRAY and SATO 1953). With the reservation that the comparison applies to a warm-blooded animal, it may be assumed that the minimum period of excitation for the receptors studied is of the same order; the moment of maximum deformation, from which the latency values used for calculating the conduction velocity were measured, would then be the most probable one for the initiation of the impulse on strong supraliminal stimulation (*cf.* Fig. 2). If it is assumed that the minimum delay is longer for the toad than for the cat by, say, one millisecond, the error in the velocity determinations will probably not exceed 10 per cent.

Receptor mechanism. The change in latency on varying the stimulus strength (Fig. 9, p. 24) and the alterations in threshold observed after subliminal stimulation (Fig. 16) are both evidence of a graded change in excitability at the receptive nerve ending. To judge from the negative effect of subliminal stimulation of neighbouring receptors (p. 48) this change would not spread as far centrally as to the level of the branching of the afferent fibre, and most probably it is confined to the receptor region. The graded character and the time course of the local change in excitability prompt a comparison with the generator potential of the pacinian corpuscle in the cat's mesentery, and for the purpose of this discussion analogies will be drawn with the results obtained in various studies on this corpuscle.

The generator potential in the pacinian corpuscle displays a refractory state, and a period of about 25 msec is required for full recovery (GRAY and SATO 1953; *cf.* LOEWENSTEIN and ALTAMIRANO-ORREGO 1958). It may be suggested that the rise in thresh-

old observed after subliminal stimulation (Fig. 16*A*) is a consequence of a corresponding refractory state in the mechanoreceptors under study. On the other hand, a *lowering* of the threshold (Fig. 16*B*) would be obtained if the graded increase in excitability induced by the conditioning stimulus persisted and supplemented the change due to the test stimulus, in the same way as successive generator potentials are additive (ALVAREZ-BUYLLA and DE ARELLANO 1953; GRAY and SATO 1953; *cf.* GRAY and MALCOLM 1950). Curves with an intermediate course, which were also encountered, may represent an approximate balance between refractoriness and an increase in excitability due to an additive effect.

It is likely that the delay in the initiation of the impulse at low stimulus strengths can be largely accounted for by utilization time of the nerve ending. This period will be reduced as the amplitude of the graded change in the receptor increases with the amplitude of displacement. The graded change may also rise more steeply on stronger stimulation, as does the generator potential in the pacinian corpuscle (GRAY and SATO 1953), and this will further reduce the latency. CATTON (1958) suggests that shifting of the origin of the impulse along the fibre ending considerably influences the latency owing to the slow conduction in the peripheral branches. However, the fact that the differences in latency displayed by the various receptors of a unit (Fig. 10*B*) were only slight may suggest that shifting of the origin, though relevant, is of minor importance for the delay in these mechanoreceptors.

It is reasonable to assume that the local change in excitability is associated with a graded potential, but the parallels drawn with various results of studies on the pacinian corpuscle do not necessarily imply that the receptors studied have a generator potential similar to that displayed by the pacinian corpuscle. The parallels actually refer to the changes in excitability that accompany the generator potential of this corpuscle. In the absence of a special receptor structure, as is probably the case for the mechanoreceptors studied, such changes in excitability may be due to the direct effect of the pressure on the receptive nerve ending, the neural structure itself being responsible for the transformation of mechanical to electrical energy (*cf. e.g.* KATZ 1950).

Variations in excitability. As suggested above (p. 26), the fluc-

tuations in threshold with time may be due to spontaneous variations in excitability—for instance, in the receptive nerve ending (*cf.* KATZ 1950, p. 259). Alternatively, the explanation may lie in dromic impulses travelling along sympathetic fibres to the skin, since such impulses have a facilitatory effect on tactile endings (LOEWENSTEIN 1956a). A varying discharge from the sympathicus during the course of an experiment may tentatively be assumed to give rise to threshold variations of the type found. In the case of receptors with constant threshold this discharge would be either constant or completely absent. Although antidromic stimulation of the fibres from the receptors under test was not followed by any long-term changes in excitability (p. 27), it would seem that an effect of antidromic discharge in small fibres, in analogy with HABGOOD'S (1950) results (see p. 26), cannot be excluded as a third explanation of the fluctuations.

The threshold became lower when the compressibility of the underlying tissues was reduced (*cf.* BÉKÉSY 1939) and this may explain why the threshold was on average lower for distal units, the compressibility being less on, for instance, the digits than more proximally. For the individual receptor the compressibility of the underlying tissue was, however, not a reliable index of the threshold level; high values were sometimes found on the digits, and low thresholds—for instance, less than 20 μ—were encountered on the calf, where the subcutaneous tissue is loose.

Since the various receptors displayed differences in threshold that could not be attributed to temporal fluctuations, differences in the compressibility of the underlying tissue or errors in the method of threshold determination, it can be concluded that there are individual differences in the excitability of the various receptors. The threshold variations were largely randomly distributed and fairly large. In the whole material the threshold varied from less than 10 μ to more than 500 μ, and within a particular unit differences of up to about four times the lowest value were recorded. The wide range of the threshold values for various receptors should be seen against the background of the fact that all the determinations were made with a stimulus of short duration. GRAY and MALCOLM (1951) have found that the threshold of touch receptors in the frog's skin is generally slightly higher for

short mechanical pulses than for those of infinite duration, and it is conceivable that the threshold differences found in the present study would have been smaller had the mechanical pulses had a longer duration. The high-threshold receptors may have had particularly slowly reacting receptor mechanisms and therefore failed to initiate propagated impulses on stimulation at low amplitudes. Possibly, the threshold differences would also have been less if the deformation of the skin had been tangentially directed (*cf.* CATTELL and HOAGLAND 1931, p. 396, and BÉKÉSY 1939, p. 322). On this point the results of the experiments with *manual* stimulation yielded complementary information. The fact that manual tactile stimulation of various receptors gave rise to bursts that differed in duration and impulse frequency implies that differences in excitability were also found when the stimulus was of longer duration and the displacement included a lateral component. These results seem also to justify the use of the threshold value obtained on vertical stimulation with short pulses as an index of the excitability in mechanoreceptors of the type studied, at least for the purpose of comparison.

Recovery of excitability. Following the initiation of a single impulse there was an absolute refractory period of 3—6 msec and a subsequent relative decrease in the excitability, which lasted 200 msec or more. These values are considerably greater than those for the post-spike decrease in excitability in A fibres of the frog, determined by means of electrical stimulation. The refractory period of these fibres is usually less than 10 msec, even in freshly isolated nerves (GRAHAM 1934). The length of the refractory period varies with the conduction velocity (BLAIR and ERLANGER 1933, Fig. 12) and may be greater for slow A fibres, but for none of the fibres included in the present study, which had a conduction velocity of 5—24 m/sec, would it reach 20 msec (see ERLANGER and GASSER 1937, p. 49). Although the subnormal period of nerve fibres is generally appreciably longer than their refractory period, A fibres in the frog may not show any late decrease in excitability at all after a brief single shock to an unpoisoned nerve (GRAHAM 1935; *cf.* GASSER 1935 and LORENTE DE NÓ 1947, p. 361), and in any case it would be of too low degree to account for the decrease found in the present study. However, in respect of the course and

duration, this decrease suggests a comparison with subnormality in C fibres which is well developed and of long duration (GASSER, RICHARDS and GRUNDFEST 1938; *cf.* ERLANGER and GASSER 1937, p. 180). Moreover, the increase in threshold on repeated mechanical stimulation of a touch receptor was cumulative, as is subnormality on repeated electrical stimulation of a nerve trunk (GRAHAM 1935; GASSER 1935; GASSER and GRUNDFEST 1936). The positive after-potential, which is related to the subnormality, is also cumulative, and the resemblance between the curve described by the summed positive after-potentials (see *e.g.* GASSER 1939, Fig. 5) and the course of the cumulative increase in threshold for a touch receptor (Fig. 20) during repeated stimulation is especially suggestive. The possibility that the decrease in excitability found on adequate stimulation of a receptor reflects the subnormal period of the nerve fibre may imply that the post-spike events known from studies on the axons of a nerve trunk are one of the factors which determine the threshold for the initiation of the sensory discharge.

A comparison between the endings studied and C fibres is prompted by histological evidence, as well as by the slow recovery, since they are thin and unmedullated, and further by the finding that the conduction velocity is low peripherally (MARUHASHI et al. 1952; CATTON 1958). All this evidence implies that the initiation of impulses is dependent on neural elements with characteristics that differ considerably from those of the afferent fibres in which the impulses are transmitted centripetally. It should be pointed out, however, that this does not seem to apply to all types of receptors. In, for instance, the pacinian corpuscle in the cat's mesentery, where each fibre generally innervates only one receptor and seldom divides outside the corpuscle, the impulses are initiated directly in myelinated and coarse fibres (QUILLIAM and SATO 1955; DIAMOND, GRAY and SATO 1956); accordingly, the recovery time is short (GRAY and MALCOLM 1950; LOEWENSTEIN and ALTAMIRANO-ORREGO 1958).

The transformation of a continuous stimulus applied to a sense organ into a repeated discharge may be explained on the basis of relative refractoriness in the nerve endings. These would fire at a certain moment during the recovery period, depending on the intensity of the stimulus (ADRIAN and ZOTTERMAN 1926b). Since the refractory period for the afferent fibres is comparatively short, special properties have been suggested to account for the initiation of the low-frequency discharges, which may be obtained from various types of receptors. The assumption that the explanation may lie in longer recovery times for the endings (BRONK 1934, p. 70; RUCH 1955, p. 309) is supported by ADRIAN and ZOTTERMAN's (1926b) calculations of the recovery cycle for stretch receptors in the frog's sternocutaneous muscle, and furthermore by the present findings. As far as can be judged from results obtained on mechanoreceptors of the type studied, the recovery process may explain frequencies down to 3 per second (length of recovery cycle up to 300 msec).

If it is postulated that the increase in excitability at 10 msec (Fig. 15) found for a number of receptors is a physiological event, and not confined to the form of stimulation used, the recovery cycle may also be a factor by which a certain firing frequency is favoured. Preliminary experiments, devoted to a closer study of the relation between threshold and frequency, were suggestive on this point. For some receptors the threshold for discharge (for short periods) at the frequency of 100 per second was *lower* than for the frequency of 70 per second. The significance of the recovery cycle in the mechanism of repeated discharge in sensory fibres is still unresolved, however, as account needs to be taken of such factors as autorhythmic properties in the receptor mechanism or fibre ending.

The deviations from the smooth course which were seen in several recovery curves and had a form indicating a superimposed damped oscillation are difficult to interpret. The course of the first deviation, which represents an increase in excitability at 10 msec after initiation of an impulse, and which was sometimes the only conspicuous deviation, suggests that it corresponds to the supernormal period in the nerve fibre (GRAHAM 1934; GASSER and GRUNDFEST 1936). The occurrence of more than one peak in the same curve does not seem to rule out the possibility that they are an essential feature of the post-spike excitability cycle. It may tentatively be suggested that they may be accounted for by an oscillation between negative and positive after-potentials (*cf.* GASSER and GRUNDFEST 1936, p. 116, LEHMANN 1937 and LORENTE DE NÓ 1947, p. 293). Interestingly enough, LOEWENSTEIN and ALTAMIRANO-ORREGO (1958) have recently described a facilitatory period in the pacinian corpuscle at an interval of 7—10 msec after mechanical stimulation. It was seen only when the conditioning stimulus was strong enough to elicit a propagated potential. However, the oscillation found in the present investigation was also observed after subliminal mechanical stimulation and this seems to indicate that it is associated with the stimulus rather than the propagated impulse. It may then be assumed that the rapid deformation sets up an oscillation—mechanical or electrical—within the skin. An electrical oscillation may occur in the membrane of the nerve ending or possibly in the dermo-epidermal membrane. There is a potential of 100 mV across the latter membrane (see *e.g.* OTTOSON, SJÖSTRAND, STENSTRÖM and SVAETICHIN 1953), and the nerve endings pass through it before their termination.

A capacitance interference from residual oscillations in the mechanical stimulator can be ruled out as an explanation of the oscillatory component of the recovery curves, since the preparation was earthed. Moreover, the residual oscillation of the stimulator rod, as well as that of the surface of the skin, were of appreciably shorter duration and different frequencies (Figs. 2, 4 and 15).

Peripheral interaction. The results strongly indicated that the increase in threshold displayed by the various receptors in a receptive field on supraliminal stimulation of one of them was caused by antidromic discharge in the peripheral fibre branches. The interaction described by CATTELL and HOAGLAND (1931) and TOWER (1940) was also inhibitory and is most probably due to the same process. There is thus evidence that at least two kinds of peripheral units are similarly organized with regard to peripheral interaction—namely, those responding to mechanical stimulation in the cornea of the cat, and the touch units in the frog and the toad.

The demonstrated distribution of the increase in threshold throughout a receptive field, implying as it does that the various receptors of a unit largely reflect the changes in excitability displayed by the receptor first stimulated, provides a logical explanation of why one receptor only fired the afferent fibre when two receptors belonging to the same unit were stimulated repeatedly (Figs. 26 and 27). When two receptors, R_A and R_B, are stimulated at different frequencies, the impulses elicited in R_A—at the lower of the two frequencies—will cause a certain increase in threshold at R_B. The strength of the stimuli applied to R_B are adjusted to make this receptor to follow a *higher* frequency and will offset the increase in threshold distributed from R_A. Once a discharge has been elicited from R_B, there will be an increase in the threshold at R_A which, however, renders the stimuli at this receptor subliminal, since their amplitude was adjusted to the lower frequency. Owing to the interaction, therefore, no discharge will be set up at a receptor as long as impulses are initiated at a higher frequency at another receptor in the field, even if the afferent fibre, having a lower degree of refractoriness, would in theory be capable of carrying the sum of the frequencies. Hence, if several receptors are stimulated simultaneously, the one that at any given moment can

set up the highest frequency will alone determine the discharge in the afferent fibre.

A similar argument may be advanced in interpreting the result of stimulating two different receptors simultaneously at the same frequency. Of each pair of stimuli only one will give rise to an impulse in the afferent fibre irrespective of the relative phase of the two stimuli, and the frequency in the fibre will not exceed that when the receptors are stimulated separately. The results were in principle the same when manual stimulation was used instead of the mechanical stimulator, the duration and frequency of the discharge being similar on separate and simultaneous touch of two receptors belonging to the same unit.

Since only one receptor at a time fires the afferent fibre the discharge on simultaneous stimulation of two or more receptors of a particular unit will be similar to that which would be obtained had the unit had a single receptor. The arrangement with several receptors connected to one fibre, however, constitutes a spatial safety factor. (This was pointed out by ADRIAN and ZOTTERMAN [1926a, p. 482] who suggested that different end-organs might interact and discussed the possible consequences.) The larger the field, the greater the probability that the unit will be activated by an arbitrarily located stimulus. Overlapping will also increase with the area of the receptive field (*cf.* Figs. 32A_U and B_U, p. 75). Furthermore, a tangentially directed stimulation of a large field may result in a discharge of longer duration and higher frequency, probably owing to a gradual recruitment of new receptors which successively fire the afferent fibre (p. 58).

Intensity discrimination. The largely random variation in excitability from one receptor to another would seem to decrease the accuracy with which the afferent discharge will signal the intensity of the stimulus. Stimuli of similar strength may, for instance, elicit discharges of different frequencies and durations in different fibres.

It is conceivable that the overlapping of the receptive fields compensates for these variations. To judge from the present results most sensitive points are innervated by several units and even a localized stimulus will therefore initiate a discharge in several afferent fibres. The receptors at a particular point may function

independently (p. 60), so it can be assumed that the discharges in various fibres differ even when they are elicited from the same sensitive point. However, the *total* number of impulses in all fibres activated by stimulation at a particular point may be approximately the same when different points are stimulated at similar intensities. Hence, the overlapping may result in a smoothing out of the individual variations in the excitability of the receptors. The only requirements of this argument that were not experimentally demonstrated are: that the variations in excitability for the receptors at a particular point reflect the variations in excitability for a sample of receptors, and that the central nervous system is capable of discriminating between mean discharges of groups of fibres.

Somatotopic localization and spatial discrimination. RUCH (1955, p. 324) has recently discussed the neural basis of localization and two-point discrimination and has combined various earlier views and data. The basis of these sensory functions will be taken up for further discussion here, since the present results seem to add new premises as regards the peripheral impulse pattern.

The discovery by TOWER (1940) that the threshold is lower and the adaptation slower in the middle of the corneal unit field than at the periphery suggests that a spatial discrimination may be possible *within* the peripheral unit. To judge from the present results there is no such discriminatory mechanism within the peripheral tactile unit in the toad. The threshold and the latency varied irregularly in the receptive field. Moreover, no consistent difference in the duration and impulse frequency of the discharge was found when various differently located receptors in a field were activated by manual stimulation.

Since the discharge in a particular afferent fibre of the type studied evidently does not indicate the locus of a stimulus within the field, it would be impossible, by means of an analysis of the response in a single peripheral unit, to define a point on the skin to a higher degree of accuracy than the greatest diameter of the receptive field. A more accurate localization of the stimulus, and hence a higher degree of discrimination, may be achieved through overlapping (*cf.* BISHOP 1946), and this will now be discussed in the light of the present findings with the aid of schematic draw-

ings. In Fig. 32, A_U is a vertical section through the skin *(thick horizontal line)*, with a number of touch fibres *(thin vertical lines)*, whose field diameters are indicated by the bifurcation turned towards the skin. The fibres are assumed to be regularly spaced and the receptive fields to be circular and of the same size for all units. Owing to the overlapping, a point stimulus S_1 will activate several fibres, of which four (indicated by *dots)* are seen on the vertical section. From A_L, which is a section parallel to the skin and corresponds to a cross-section of the skin nerve, it is seen that a total of 16 fibres (represented by *dots)* are fired by S_1. When the point stimulus is moved to S_2, the activity will pass to a new set of fibres *(crosses)*. It is conceivable that such a shift of activity from one set of fibres to another—in this case implying that 12 new fibres are activated—will be sufficient for discrimination of S_1 and S_2, although the space between the two stimuli is *less* than the diameter of the receptive field.

The influence of the size of the receptive fields is evident from a comparison with Figs. 32B_U and B_L, in which the premises are the same as in A_U and A_L, except that the area of each field is 50 per cent greater. Plotting of the fields shows that each stimulus will now activate six fibres seen on the vertical section (B_U) and a total of 32 fibres (B_L). The number of new fibres thrown into activity when the stimulus is moved from S_1 to S_2 will also be greater (18). An increase in the size of the receptive field, alone, would therefore not necessarily reduce the discriminatory power. Too large fields may, however, result in poorer spatial discrimination, since when the field area is increased the change in the number of active fibres on moving the stimulus will decrease *in relation to* the total number activated at a particular point (*cf.* Figs. 32 *A* and B_L).

A shift of activity of the type described may constitute the background for spatial discrimination when a number of points are stimulated in succession, as when an object moves on the skin. What then are the prerequisites for discrimination of two stimuli applied *simultaneously*? If the two stimuli S_1 and S_2 in Fig. 32 A_U or B_U are applied simultaneously, the fields of the middle fibres will be affected by *both* S_1 and S_2. Owing to the peripheral interaction, however, the discharge from only one of the

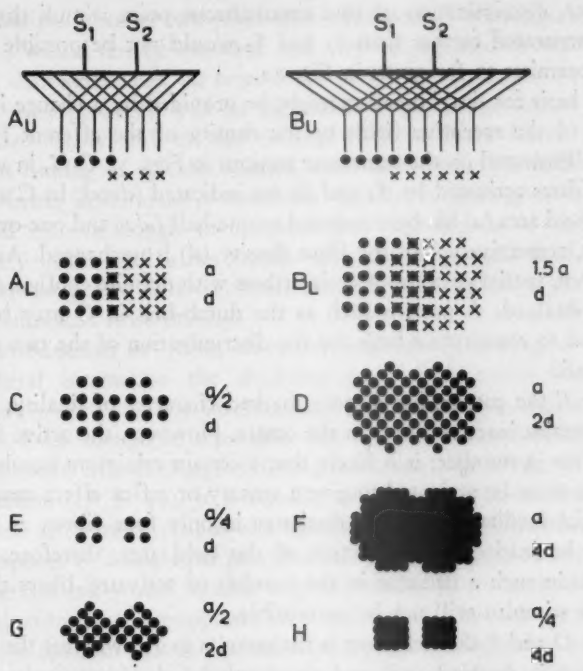

Fig. 32. Activity patterns in afferent fibres (*thin vertical lines*) in response to two mechanical point stimuli (S_1 and S_2) applied to skin surface (*horizontal thick line*). A_U and B_U show the active fibres seen on a vertical section at stimulated points. Fibres marked by ● and x are activated by S_1 and S_2, respectively; A_L and B_L are sections parallel to the skin corresponding to cross-sections of the nerve trunk and showing all fibres activated by S_1 and S_2. *C—H:* Cross-sections showing patterns set up by S_1 and S_2 when receptive area (*a*) and density of afferent fibres (*d*) are varied.

stimuli will be transmitted in each fibre, and the response will be the same in the middle fibres as in the fibres whose fields are subjected to either S_1 or S_2. The question is now whether the activity pattern in Fig. 32 A_L or B_L is specific for the two point stimuli. If these are replaced by *one* stimulus that is edge-shaped and deforms the whole stretch between the points previously stimulated by S_1 and S_2, the same fibres will be activated, and the discharge in each fibre will be the same as on point stimulation.

Hence, discrimination of two simultaneous point stimuli that are not separated farther than S_1 and S_2 would not be possible with the premises so far given in Fig. 32.

A basis for discrimination might be provided by a change in the area of the receptive fields or the density of the afferent fibres, as is illustrated on the transverse sections in Figs. 32 *C-H*, in which the fibres activated by S_1 and S_2 are indicated *(dots)*. In *C* and *E* the field area *(a)* has been reduced to one-half *(a/2)* and one-quarter *(a/4)*, respectively, but the fibre density (*d*) is unchanged. As will be seen, spatial patterns of active fibres with definite configurations are obtained. A pattern such as the dumb-bell in *C* may be assumed to constitute a basis for the discrimination of the two point stimuli.

In *E* the pattern has a more marked character of duality, since it contains inactive fibres in the centre. However, the active fibres are few in number; it is likely that a certain minimum number of fibres must be activated to give a sensory or reflex effect centrally (spatial facilitation), and a discharge in only four fibres, as in *E*, may be inadequate. Reduction of the field area, therefore, may result in such a decrease in the number of activated fibres that a point stimulus will not be perceptible.

In *D* and *F* the field area is the same as in A_L whereas the fibre density is doubled *(2d)* and quadrupled *(4d)*, respectively. This variation also gives something of a dumb-bell form to the peripheral pattern. In *G* and *H* the field area has been reduced *and* the fibre density increased; evidently, this combination of changes is most likely to increase the specificity of the peripheral pattern. The patterns in *G* and *H* both have a markedly dual character, and each stimulus elicits an adequate number of fibres.

The significance of the peripheral patterns is, of course, dependent on changes which they may undergo during the afferent transmission and ultimately on the analysis at high levels. A temporal dispersion occurs already in the periphery on account of the differences in the conduction velocity of the afferent fibres, and in the central nervous system the patterns may be transformed at the various synaptic levels. In view of this, as well as the above discussion on field size, fibre density and spatial patterns, such a finding as a direct agreement between the diameter of the unit

field and the limen of two-point discrimination (*cf.* WEDDELL 1941, p. 362) would not be expected and may be regarded as random, rather than systematic. As regards the peripheral arrangement, this limen most probably will be dependent both on the size of the receptive fields and on the density of the afferent fibres. The present finding of apically located small units (p. 21) would suggest a better discriminative sensibility distally, in analogy with the case in man, although the physiological significance of such a property in the toad is not readily apparent. The small field area may be one prerequisite for better discrimination apically, another being increased fibre density.

Discrimination of form, direction and speed. Owing to the peripheral interaction the discharge in a single tactile fibre is unlikely to provide any information on the size of a stimulating object. Even though it is possible that a tangentially directed stimulus results in a discharge differing from that elicited by vertical application (*cf.* p. 58), it is equally unlikely that discrimination between different directions of a stimulus can be reliably based on the response in a single peripheral unit. A vertical pressure applied at a certain rate would be able to give a similar discharge to a tangential stimulus of appropriate form and speed. Moreover, a short duration stimulus that is allowed to move across the field at a low velocity may be assumed to give the same response as a stimulus of higher speed but slightly longer duration.

Concluding remarks. On the basis of the experimental results it is suggested that, as far as the toad is concerned, information that is essential for discriminative sensibility, such as the extent of the stimulus on, and the direction of motion in relation to the surface of the skin is, like the exact somatotopic localization, obtainable only on the basis of activity in several units—that is, spatio-temporal impulse patterns. As regards intensity discrimination, the overlapping may compensate for the inaccuracy that might be expected to arise from the differences in excitability displayed by various receptors.

SUMMARY

1. An investigation has been performed on peripheral sensory units with low-threshold, rapidly adapting mechanoreceptors (touch receptors). The material consisted of decerebrated toads, the receptors examined being located on the lower leg and the foot. Discharges in single afferent fibres were studied by recording from thin dorsal root filaments. Single receptors were stimulated with short mechanical pulses of known shape (Fig. 2) and variable amplitude (0—500 μ). The stimulus strength was expressed in terms of the vertical displacement of the surface of the skin, which was recorded on each stimulation by means of a capacitance meter. As found in control experiments, the displacement was localized (Fig. 3) and the recovery of the skin rapid (Fig. 4). In some tests manual tactile stimulation was used.

2. The receptive fields were generally irregular in shape. Most of the fields were 2—35 sq. mm and contained 2—29 point-like regions, stimulation at each of which elicited a discharge in the afferent fibre. The sensitive points were usually separated by a zone of "insensitive" skin and located each on one wart (Figs. 5, 6 and 10).

One sensitive point is regarded as representing a single receptor, which probably consists of the free ending of a branch of the afferent fibre.

Some units had small receptive fields about one square millimetre in area. These units were found only at the tips of the digits and the poles of the pads (Fig. 7).

3. The application of threshold or supraliminal mechanical pulses to single receptors elicited single impulses in the afferent fibre. The thresholds varied considerably from one receptor to another, most of them being between 10 and 150 μ (vertical displacement of the skin surface). Even for receptors belonging to the same unit differences were found, although the range was smaller (Fig. 10*A*). The threshold of a particular receptor was not related to its position within the field.

Certain factors influencing the threshold were studied. Both low and high thresholds were found in all regions of the hindleg examined, but, on the average, the threshold was lower for units whose receptive fields were partly or wholly located on the digits. The threshold was lower when the skin was allowed to rest on a firm instead of a loose base. For several receptors the threshold varied with time.

4. The latency-shortening effect of supraliminal stimulation was confirmed (Fig. 9). The shortest latency differed slightly for receptors belonging to the same unit (Fig. 10*B*); the value for a particular receptor was not related to the position of the receptor within the receptive field nor to its threshold.

The average conduction velocity for the stretch between the receptor and the spinal cord was calculated for 97 units (Fig. 11). The values lay between 5 and 24 metres per second, with a fairly uniform distribution within these limits, the mean being 12 metres per second.

5. (i) The changes in excitability induced by a single *threshold or supraliminal* mechanical pulse were examined by determining the threshold for the discharge of a second impulse from the *same* receptor. There was an absolute refractory period of 3—6 msec. The subsequent recovery, which generally lasted for more than 200 msec, described a curve of the hyperbolic type (Fig. 14). In one-half of the cases variations were encountered in the recovery curve, the most conspicuous of which was an increase in excitability after 10 msec (Fig. 15). On repeated supraliminal stimulation there was a cumulative increase in threshold (Fig. 20).

(ii) On single or repeated *subliminal* stimulation of the *same* receptor the threshold was sometimes elevated or lowered at short intervals, but the change never lasted longer than 20 msec (Fig. 16).

(iii) Following *antidromic* stimulation of the afferent fibre in the dorsal root there was a graded increase in threshold for the various receptors of the unit. For each receptor the course of the recovery was similar to that after supraliminal mechanical stimulation of the same receptor (Fig. 18).

The courses of the various recovery curves provide evidence that the fall in the excitability of a receptor after supraliminal mechanical stimulation is a consequence of the propagated impulse

and is not due to refractoriness in the receptor mechanism. It is pointed out that the recovery of the endings is slower than that of the afferent fibres in the nerve trunk. The time course and the cumulative property of the fall in excitability on supraliminal mechanical stimulation prompted a comparison with the sub- and supernormal periods of nerve fibres.

6. On *threshold or supraliminal* stimulation (either single or repeated) of *another* receptor belonging to the same unit the excitability was reduced to much the same extent as on stimulation of the receptor under test (Fig. 21). There was a similar fall in excitability for all receptors of a unit when one of them was stimulated.

For each receptor the recovery curve after stimulation of another receptor of the unit agreed with the curve for antidromic stimulation. This is indirect proof that the fall in excitability distributed to the various receptors of a unit is due to antidromic impulse discharge from the site of branching of the afferent fibre. This mechanism will take the form of a mutual inhibitory interaction between the receptors of a unit when two or more of them are stimulated simultaneously.

7. The excitability of a particular receptor was not influenced by *subliminal* stimulation of *another* receptor of the unit. Simultaneous stimulation of two receptors, each at subliminal strength, elicited no response in the afferent fibre—that is to say, subliminal stimuli were not additive. The threshold was uninfluenced by the adaptation of other receptors in the field by applying constant pressure.

These results indicate that adaptation and subliminal changes in excitability are localized phenomena which at least do not spread beyond the particular fibre branch whose end is stimulated.

8. When two receptors belonging to the same unit were stimulated repeatedly at different frequencies, each receptor at the threshold amplitude for the particular frequency used, only impulses from the receptor stimulated at the higher frequency were transmitted in the afferent fibre (Fig. 26). When two receptors were stimulated at frequencies that were practically equal the afferent fibre fired at a similar frequency (Fig. 27). Hence, only one receptor at a time discharged the afferent fibre; this could

readily be explained on the basis of the demonstrated interaction between the receptors of a unit. The chief mechanism of integration of activity released in various peripheral branches of a single afferent fibre is to be found in these results.

9. In experiments with *manual* tactile stimulation of single receptors, the duration and impulse frequency of the discharge was determined. Different values might be obtained for different receptors, even for those belonging to the same unit. The differences were, in the latter case, apparently not related to the position of the receptors in the receptive field.

The values obtained on simultaneous touch of two receptors belonging to the same unit were substantially the same as those obtained by separate stimulation of one of the receptors. This indicates that the mechanism of peripheral interaction, as analysed by means of the mechanical stimulator, also applies during natural touch stimulation.

10. It was confirmed that touch units overlap extensively. A particular sensitive point was usually innervated by several units. In a limited number of experiments, in which two activable touch fibres with overlapping receptive fields were found in the same dorsal root filament (Fig. 30), attempts were made to demonstrate interaction between the *units*. There was no evidence of interaction in connection with the initiation of impulses at a common sensitive point (W_{AB} in Fig. 30), or during the afferent transmission (Fig. 31).

11. The peripheral neural basis of discriminative sensibility is discussed. As no mechanism for spatial discrimination within the peripheral unit could be demonstrated, it is assumed that this sensory function is dependent on the activity in several units—that is, on spatio-temporal impulse patterns. As regards intensity discrimination, the inaccuracy that might arise from the individual differences in the excitability of the receptors may to some degree be compensated by the overlapping of the receptive fields of several units.

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